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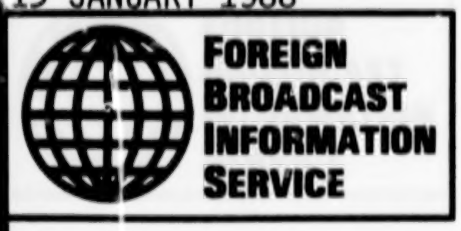

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COMBINED EFFECT OF MICROWAVES AND IONIZING RADIATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (manuscript received 3 Mar 87) pp 4-9

[Article by Yu. G. Grigoryev, V. S. Stepanov, G. V. Batanov, L. I. Beskhlebnova, Z. Ya. Mityayeva, A. A. Paramonov and R. M. Salimov]

[English abstract from source] The response of different physiological systems to ionizing radiation as modified by UHF radiation of nonthermal intensity was investigated. The experimental rats were exposed to electromagnetic irradiation of the power flux density (PFD) 200 $\mu W/cm^2$ 30 min daily for 8 days and the next day they were exposed to single total-body gamma-irradiation at a dose of 5.5 Gy. Pre-exposure to UHF irradiation reduced 1.5 times the mortality rate of the test animals as compared to the controls. Immunobiological examinations revealed a significant increase of the stimulation index in the mitogen (PHA) induced lymphocyte blast-transformation reaction and a decrease of the autopatch count. The motor activity of the rats exposed for 20 min to gamma-irradiation at a dose of 0.34 Gy and the next day to UHF irradiation (PFD = 40 $\mu W/cm^2$) for 1 and 5 min remained essentially unchanged. The imprinting of the chicks irradiated in early embryogenesis for 5 min with UHF (PFD = 40 $\mu W/cm^2$) and then with gamma-rays at a dose of 0.36 Gy was disrupted.

[Text] In recent times, investigation of the combined effect of nonionizing and ionizing radiation as an environmental factor has gained increasing importance. Such studies are particularly important in the development of criteria of radiation safety of manned spaceflights.

Previously, questions of prediction of the biological effect of a combination of physical environmental factors were discussed in special surveys [1-2]. Here, we intended to furnish a description of some of the general physiological responses to various physical factors and demonstrate the distinctions of the biological effect of each factor. Microwaves and ionizing radiation were the main factors, and the latter was also used as a "test factor" in order to demonstrate the sought effect.

It was previously [1, 2] shown that, regardless of the type of prior exposure (moderate hypoxia, angular and Coriolis' accelerations, stationary

magnetic field), there is development of greater resistance to ionizing radiation. We obtained an analogous effect, according to the criterion of animal mortality, after pre-exposing animals to electromagnetic fields in the microwave range.

The studies were conducted on 54 white, mongrel female rats with a base weight of 155±16 g. The experimental group (18 rats) was exposed to an electromagnetic field for 30 min/day for 8 days. The frequency of electromagnetic radiation used in the experiment was 9340±10 MHz (wavelength λ = 3.2 cm). Power flux density (PFD) at the location of the animal over a 20×20 cm area constituted 200±25 μW/cm^2. Nonuniformity of intensity was 30%. Polarization of the field was linear, with orientation of vector E parallel to the platform with the animals (they were irradiated from the top). Ambient temperature in the zone of radiation was 21±0.5°C. Humidity and illumination in the area of experimental and control groups of animals were maintained at about the same levels in all cycles of exposure to electromagnetic radiation. Subsequently, on the 9th day after the start of microwave exposure, the experimental and control (36 rats) groups were exposed once to total-body γ-radiation in a total dose of 5.5 Gy (dose rate 0.01 Gy/s).

Rats pre-exposed to microwaves showed a distinct tendency toward higher survival rate, as compared to control animals exposed only to γ-radiation. Pre-exposure to microwaves lowered mortality by more than a factor of 1.5 in the experimental group, as compared to the control.

As shown by analysis of the time-effect function for the experimental and control groups of animals, mean effective time (LD_{50}), in which 50% of the experimental animals died, constituted 26.6 days (17.7-39.9 days), whereas in the control group it was 15.4 days (12.2-19.4 days). The difference was statistically reliable ($P<0.05$).

A comparison of the obtained results to experimental data cannot fail to show that, in a number of studies, analogous results were obtained to the effect that pre-exposure to microwaves has a protective effect on the course of radiation damage [4, 5, 8]. At the same time, some authors [3, 7] observe that there is an additive effect of microwaves and ionizing radiation. It must be noted that, in all of the cited works where the effect of microwaves as related to ionizing radiation is assessed as being synergistic or additive, a considerably higher PFD level was used than in our investigation (by several orders of magnitude). On the basis of the results, it can be concluded that a general nonspecific response can develop to a combination of two physical environmental factors, and that the energy parameter of not only ionizing but microwave radiation is important.

In the experiments, we assessed the immunobiological status on the basis of two parameters at the same time: response of blast-transformation of lymphocytes in a culture of whole blood in a micromodification and response of autologous plaque production using conventional methods.

We observed significant increase in stimulation index in the blast-transformation response of lymphocytes under the combined effect of microwaves and ionizing radiation, as compared to the control, as well as the group exposed to

ionizing radiation, in which this response was depressed (Table 1). The number of autoplaques showed only a 2-fold increase in the experimental group, whereas in animals exposed only to ionizing radiation this parameter showed a 5-fold change.

Table 1. Change in immunobiological parameters (M±m) under the combined effect of microwaves with PFD 200±25 $\mu W/cm^2$ and γ-radiation in a dosage of 5.5 Gy

Parameter	Before exposure	Micro-waves	Gamma-radiation	UHF + γ-radiation
Leukocyte count, thou	12,3±0,9	16,3±0,7	1,8±0,3	1,9±0,3
Autoplaques, %	4,9±0,5	1,84±0,6	20,7±5,4	10,7±1,5
Blast-transformation reaction, stimulation index	5,42±0,46	6,4±0,4	3,13±1,1	10,1±2,75

At the present time, radiosensitivity of T-lymphocytes is well-known; however pre-exposure to microwaves was instrumental in rendering them resistant to ionizing radiation. Being an integral test for evaluation of the functional state of immunocompetent cells, the dynamics of blast-transformation responses are indicative of the body's capacity to acquire a qualitatively new response under the effect of microwaves to exposure to γ-radiation, and we view this as some specificity of biological effects of microwaves.

As yet, the mechanism of formation of radioresistance, according to such an integral parameter as animal mortality, has not been identified. We can only assume that the effect we obtained is one of the manifestations of the general adaptation-adjustment syndrome in response to repeated exposure to radiation. One of the confirmations of this is referable to data on dynamics of plaque-formation response, which is one of the indicators of the process of sensitization by the products of normal tissue breakdown.

We could discuss conditions, under which the physical environmental factors are of rather mild intensity, and it is not possible to detect an integral nonspecific reaction. For this reason, we conducted experiments to assess behavioral responses (motor activity) of animals exposed to microwaves and ionizing radiation.

To record rat motor activity and measure the parameters of trajectory of movement, we used the Optovarimex Medata (Sweden) unit, which contains an optical platform with infrared sensors of the animal's spatial position (the space is limited to the dimensions of a transparent plexiglas box, 400×400×200 mm), two-coordinate continuous automatic recorder of planar position of the animal, 8-channel counter with a digital printer reflecting the following parameters: H--integral parameter of motor activity on plane X-Y (distance traveled by the animal within the analysis time), X, Y--projection of trajectory of route traveled by animal on X and Y axis; V--number of times the animal stood up to a height of 5 cm from the bottom of the box. During measurement of motor activity, a white-noise generator was turned on, and its level constituted 67 dB.

Experiments were conducted with male Wistar rats at the same time of day, from 1400 to 1700 hours. Animals were used once in the experiment. The results were processed using 3-factor variance analysis.

The animals were exposed to 0.34 Gy γ-radiation for 20 min. They were exposed in groups of seven rats. Control animals were exposed to "pseudo"-radiation, and exposure to microwaves was 1 day after ionizing radiation (10 GHz, pulse recurrence frequency 10 Hz, PFD 40 $\mu W/cm^2$, exposure time 1 and 5 min). During exposure, the animals were in a plexiglas box (200×200×200 mm) with a foam plastic lid. Radiation was delivered from the top. The animals were delivered to the exposure site one at a time from the vivarium, where they were kept under standard vivarium conditions, 5 rats per cage. Motor activity was measured 1 min after exposure to microwaves. In all, 28 animals were used in the experiment.

Exposure to γ-radiation of the above-mentioned parameters elicited reliable ($P<0.05$) change in parameter Y of motor activity of the animals. No reliable changes were found in parameters H, X and V under the effect of γ-radiation. Exposure to microwaves of the indicated parameters for 1 min did not elicit changes in parameters of rat motor activity. We failed to demonstrate a biological effect with combined exposure to γ-radiation and UHF for 1 min.

Testing of the effect of extending UHF exposure time from 1 to 5 min, with retention of all other irradiation conditions but without γ-radiation, revealed that there is a difference between parameters H and Y in the 1st min in the control ($P<0.05$) and no difference in parameters X and V in the control. This difference is related to the existing asymmetry of the motor analyzer. In the control, parameters H and Y of motor activity differed significantly ($P<0.05$) from those found in the 2d, 3d, 4th and 5th min (also in the control), whereas such a difference was not present for parameters X and V. The greater values of parameters H and Y in the 1st min, as compared to subsequent times, is related to the predominant manifestation of exploratory activity at this time. The decline of Y, as well as H, in the 1st min in irradiated animals, as compared to the control, could be attributed to appearance of diminished exploratory activity in irradiated animals. While significant decline of activity was observed in control animals in the 2d min ($P<0.05$), in irradiated animals such a difference appeared in the 4th min ($P<0.05$). The latter could be indicative of compensatory extension of the period of becoming familiary with the surroundings. An analogous phenomenon is known to be present under stress.

The findings indicate that, when microwave exposure time is reduced to 1 min and other radiation parameters remain unchanged, no changes whatsoever are observed in the behavioral responses of rats. Additional exposure of these animals to γ-radiation in a dosage of 0.34 Gy 1 day after the microwaves does not elicit reliable change in parameters of motor activity of the rats.

In the case of attenuation of compensatory or adaptive processes, one can obtain an effect that is specific to either type of radiation. To date, sufficient data have been accumulated to the effect that microwaves and ionizing radiation have some biological effect on the nervous system. For this reason, we decided to use a special form of memory, imprinting, to obtain the so-called specific effect of the two factors we tested, microwaves and ionizing radiation in low doses.

The study was conducted with chicks divided into four groups (three experimental and one control). The first group was exposed for 5 min to continuous microwaves (9340±10 MHz, PFD 40 μW/cm^2) 24 h after the start of embryo incubation; the second group of embryos was exposed to 0.36 Gy γ-radiation; the third group was first exposed to microwaves with the same parameters as the first group then to γ-radiation in a dosage of 0.36 Gy. The fourth group of embryos was kept under the same conditions, but not exposed to radiation. In the course of incubation, a few hours before hatching, the eggs were placed in separate boxes so that there would not be mutual imprinting in the chicks after hatching. Imprinting in chicks was tested using our modification of a previously described method [6]. Chick imprinting was conducted in the sensitive period, 20-24 h after hatching, in two stages: training and testing.

Table 2. Characteristics of chick imprinting after exposure to microwaves and ionizing radiation (PFD 40 μW/cm^2; 5 min; γ-radiation dose 0.36 Gy)

Parameter	Group	Stimulus	Stimulus exposure time		Number of approaches		Number of contacts	
			number of changes	M	number of chang.	M	number of changes	M
Imprinting	1	I	37	139	38	1,8	38	3,2
	2	I	28	112	30	1,2	30	1,7
	3	I	27	141	28	1,7	28	4,2
	4	I	36	146	36	1,3	26	1,7
Testing	1	I	19	234	19	3,6	18	5,7
		D	19	105	19	1,5	18	1,6
	2	I	14	236	14	2,32	18	3,3
		D	14	183	13	2,4	14	4,5
	3	I	14	223	14	2,4	14	2,5
		D	14	165	14	4,9	14	2,8
	4	I	18	271	18	4,7	18	6,6
		D	18	113	17	1,0	18	1,3
Preference index	1		19	0,69	19	0,72	19	0,78
	2		14	0,45	14	0,53	14	0,51
	3		14	0,58	14	0,36	14	0,43
	4		18	0,70	18	0,80	18	0,79

Key: I) imprint stimulus D) differentiation stimulus M) means

Flashes of the photostimulator lamp at a frequency of 10 Hz served as the imprint stimulus. Testing for retention of the imprint stimulus was performed 24 h after imprinting, leaving one lamp to flash at 10 Hz (imprint stimulus) and the other at a frequency of 2 Hz (differentiation stimulus). In making a quantitative assessment of the response, we took into consideration the time spent near the stimuli, number of approaches and contacts with them. Imprinting was assessed according to indexes of imprint-stimulus preference, defined as the ratio, A/(A+B), where A is the parameter for imprint stimulus and B for the differentiation stimulus. The obtained data were submitted to statistical processing by the method of multiple factor analysis using Fisher's criterion. The obtained data are listed in Table 2.

The first group of chicks did not differ from controls in any of the imprinting parameters. The second group remained in the zone of the imprint stimulus for

53 s longer than in the zone of the differentiation stimulus, and the number of contacts with it was virtually the same. In the first and third groups, mean time near the imprint stimulus was longer than near the differentiation stimulus. The chicks of the third group approached the imprint stimulus even less often than the differentiated one ($P<0.05$).

The experimental groups of chicks did not differ from controls in their physical condition or appearance. With the first delivery of flashes at a frequency of 10 Hz, the control chicks remained in the zone of the imprint stimulus for a mean of 146 s; the number of approaches and contacts with it constituted 1.3 and 1.7, respectively (see Table 2). In the first, second and third groups, there was insignificant decrease to 139, 112 and 141 s, respectively, in time spend near the imprint stimulus, as compared to the control group. The number of approaches were virtually the same in experimental and control groups. Maximum number of contacts, as compared to the control group, was observed for chicks in the first (1.8) and third (1.7) groups.

Testing of imprinting revealed that control chicks remained longer in the zone of the imprint stimulus, approached and contact it more often than the zone of the differentiation stimulus. The differences between parameters for the two stimuli are statistically reliable ($P<0.05$). The first group of chicks did not differ from the control in any of the imprinting parameters. The findings were somewhat different in the other experimental groups. Thus, in spite of the fact that the second group of chicks stayed in the zone of the imprint stimulus for 53 s longer than in the zone of the differentiation stimulus, the number of approaches to both stimuli and contacts with them was virtually the same, i.e., not all chicks in this group preferred the imprint stimulus. The first and third groups spent more time on the average near the imprint stimulus than the differentiation one. The third group of chicks approached the imprint stimulus even less often than the differentiation one ($P<0.05$).

Calculation of the preference index according to all parameters revealed that it was highest in control chicks (0.70, 0.79 and 0.80). With exposure to γ-radiatio the index declined reliably ($P<0.05$) to 0.45, 0.53 and 0.51, whereas under the combined effect of microwaves and gamma radiation it dropped to 0.43-0.36 ($P<0.05$). The experimental chicks spent less time near the imprint stimulus than the controls. The number of approaches and contacts decreased reliably in the second and third groups. All of the parameters for the differentiation stimulus were higher in these chicks than the control.

The above data indicate that, upon the first presentation of the imprint stimulus motor activity diminished in chicks exposed to γ-radiation at the early stage of embryogenesis, as compared to the control, whereas exposure to microwaves led to some increase in activity, while combined exposure to γ-radiation and microwaves elicited an increase in motor activity of the chicks, as compared to both the control and those exposed to microwaves or γ-radiation alone. On the 2d day, testing revealed that motor activity was virtually the same in control and experimental chicks, whereas efficacy of imprinting varied. In the control group, 89 chicks retained the imprint stimulus, as indicated by the high preference index for all parameters, particularly number of approaches (see Table 2). The retention capacity of chicks exposed to microwaves 24 h after the start of incubation was virtually the same as in the control. In chicks exposed to

γ-radiation in early embryogenesis, the preference index constituted 0.53 for number of approaches, i.e., their capacity for retention diminished. The number of chicks that retained the imprint stimulus constituted 42.8%.

Exposure to γ-radiation and microwaves led to further loss of capacity for retention. In this group, the imprint stimulus was retained by only 21.4% of the chicks. The preference index was 0.36, i.e., preference for a new differentiation stimulus developed after exposure to the combined factors.

These data are indicative of enhancement of the effect with combined exposure of chicks in early embryogenesis to continuous microwaves with PFD of 40 $\mu W/cm^2$ and γ-radiation in a total dose of 0.36 Gy. On the basis of these studies, it can be concluded that the combination of microwaves and γ-radiation used in the period of early embryogenesis has a so-called specific effect on the central nervous system: it impairs formation of imprinting, which is a special form of memory.

Thus, the results are indicative of a possible modifying effect of low-intensity microwaves on subsequent responses of various physiological systems to ionizing radiation, development of three types of reactions to the combination of ionizing and nonionizing radiation: increase in general reactivity, compensation of functional changes on the systemic and organism levels, intensification of specific effects.

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

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EXPERIMENTS WITH RATS FLOWN ABOARD COSMOS-1667 BIOSATELLITE (MAIN OBJECTIVES, CONDITIONS AND RESULTS)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (manuscript received 8 Dec 86) pp 9-16

[Article by O. G. Gazenko, Ye. A. Ilyin, Ye. A. Savina, L. V. Serova, A. S. Kaplanskiy, V. S. Oganov, I. A. Popova, K. V. Smirnov and I. V. Konstantinova]

[English abstract from source] Morphobiochemical investigations of the rats flown on the biosatellite Cosmos-1667 have shown that the 7-day spaceflight produces shifts in different systems, organs and tissues which reflect adaptive processes to microgravity. Early signs of structural, functional and metabolic rearrangement can be detected in the musculoskeletal apparatus, hemopoietic system, lymphoid organs, neurohormonal systems, i.e., in the systems and organs that develop changes during long-term flights. The rates of adaptation to microgravity are different not only in various systems and organs but also within the same tissues. Most shifts that emerge at an early stage of adaptation to microgravity progress with flight time but some of them develop to a full extent after the 7-day flight. The specific feature of the early stage of adaptation to microgravity is the lack of significant changes in blood biochemistry in the presence of structural and metabolic changes in tissues. This fact gives evidence that the mechanisms maintaining homeostasis at the organism level are not as yet disrupted during 7 days of flight.

[Text] Many facts have been accumulate to date on the effect of weightlessness on rats during flights lasting 18-22 days [3, 4, 6]. Analysis of the results of these studies has shown that all of the changes observed in the animals can be arbitrarily divided into two groups, those directly related to weightlessness and those caused by acute gravity stress, which develops in rats when they change from a state of weightlessness to earth's gravity.

Morphological and biochemical changes that arise in rats during a flight show a correlation, in many respects, with physiological manifestations of human responses to weightlessness, with regard to direction, and for this reason they can be used to gain understanding of the mechanisms on which they are based. Thus, signs of deconditioning of the cardiovascular system have been observed

postflight in cosmonauts. A decline in activity of myosin ATPase and level of sarcoplasmic proteins [1, 2], reliable decrease in number and volume of mitochondria, relative volume of smooth endoplasmic reticulum, as well as early signs of atrophic changes in myofibrils [15], have been consistently observed in the rat heart following long-term flights. The aggregate of these structural and biochemical changes is indicative of decline of energy potential and contractile properties of the myocardium, and it can serve as the basis for development of myocardial deconditioning.

Until recently, we had data pertaining to virtually a single term of exposure to weightlessness. For this reason, experiments with animals (monkeys and rats) during short-term flights are of great interest. Such experiments make it possible to expand significantly the range of information concerning processes in mammals at the early stage of adaptation to weightlessness and, consequently, deepen our understanding of the mechanisms of physiological changes observed in the first few days of exposure to microgravity. Heretofore, conceptions of mechanisms of responses arising at the early stage of flight were based on clinical observations, results of physiological and biochemical (peripheral blood, urine) studies. Experiments aboard the biosatellites Cosmos-1514 (5-day flight) and Cosmos-1667 (7-day flight) have, to a large extent, filled the gap in our knowledge about this period of adaptation to weightlessness.

The basic objectives of the experiment with rats aboard Cosmos-1667 were: to establish the early signs of structural and metabolic changes in the basic vital systems and organs and, on this basis, to assess the processes in mammals that occur at the early stage of adaptation to weightlessness; comparison of results obtained in short- and long-term flights in order to assess the dynamics of processes of adaptation to weightlessness.

Proceeding from the goals set forth, a morphobiochemical program was formed for postflight examination of animals, which included both traditional (used in prior biosatellites) and new investigative methods. In particular, electron microscopy was performed for the first time in this experiment for examination of different parts of the brain, thyroid and parathyroid, with identification of hormone receptors in different parenchymatous organs.

In addition to Soviet scientists, specialists from the People's Republic of Bulgaria, Hungarian People's Republic, GDR, Polish People's Republic, Socialist Republic of Romania, CSSR and France participated in developing the experimental protocol and examining the animals.[1]

The experiment performed aboard Cosmos-1667 was conducted in the period from 10 to 17 July 1985. We used adult (100 days old) male Wistar-SPF rats (free of pathogenic flora) furnished by the Institute of Experimental Endocrinology, Slovak Academy of Sciences (Bratislava, CSSR). The animals were selected and prepared according to a previously developed method, which was modified to suit the duration and conditions of preparing for this experiment [13].

We used 10 rats in the flight experiment, and they were kept in one Bios-Vivarium cage (see Figure); they were fed special pasty feed [9] at the rate

[1]The data obtained in this experiment will be furnished in detail in separate publications.

General appearance of Bios-Vivarium

of 55 g/day/animal, and the rats had access to water at all times.

A ground-based control experiment was conducted from 9 to 15 August (30 days after the start of the flight experiment) in a mockup of the biosatellite, where inflight animal upkeep conditions and physiologically significant factors related to launching and landing the space vehicle were simulated. Rats of the same age as in the flight group, but from a different batch, were used in the ground-based experiment. For this reason, for each of these experiments, vivarium control rats from the appropriate batch were decapitated.

Seven of the 10 rats used in the flight experiment were decapitated 4-8 h after the biosatellite landed; 3 rats were used to test postflight reproductive function. The same number of animals was tested in each control group. All of the animals were decapitated using a guillotine at the same time of day between 0930 and 1300 hours.

After opening the Bios-Vivarium container where the rats were kept during the spaceflight, it was determined that their general condition was quite satisfactory. During decapitation (4-8 h after returning to earth's gravity) we were impressed by the listlessness and passivity of the rats: they did not resist to being handled and did not try to escape. The impression was gained that, in spite of the shortness of the flight, the animals did react to being returned to earth's gravity.

Necropsy findings warrant the belief that the 7-day spaceflight did not elicit weight loss or lead to development of macroscopically visible changes in rat organs and tissues. At the same time, weight measurements revealed that there was a reliable decrease in weight of most tested muscles, as well as thymus and spleen, while kidney weight increased, as compared to the vivarium control. Necropsy failed to demonstrate any changes whatsoever in rats used in the ground-based control experiment, and this applied to weight of above-mentioned organs as well (Tables 1 and 2). Among the distinctions noted upon necropsy on rats of the flight group, we should mention dilatation of the stomach and its overfilling with feed mass. This was not observed in rats of the ground-based control experiment, although the same amount of time (6-10 h) had elapsed after the last feeding in both experiments. For this reason, it can be assumed that short-term exposure to microgravity has an adverse effect on the function of smooth muscles, causing slower evacuation of food from the stomach. It should be noted that facts have been recently accumulated that are indicative of the need for a special investigation of the state of smooth muscles in animals following spaceflights. Thus, during the embryonic experiment aboard the preceding biosatellite, Cosmos-1514, protracted labor was noted in rats after the 5-day flight. Perhaps, impaired function of smooth intestinal muscles was also the cause of volvulus in the monkey, Bion.

Table 1. Weight of body and viscera of rats used in experiment aboard Cosmos-1667

Animal group	Body wt., g	Weight of organs, mg						
		heart	liver	kidneys	spleen	thymus	adrenals	testes
Flight	332±4	960±16	11 014±408	2460±80*	524±18*	193±14*	42.7±1.5	2410±230
Vivarium control	334±7	967±38	10 545±353	2170±70	592±27	235±14	42.5±1.4	2360±230
Ground-based control exp.	349±4.5	991±35	12 857±332*	2329±69	633±50	199±18	46.7±18	2730±91
Vivarium control	348±6.6	920±17	9 700±484	2219±68	614±24	189±17	44.4±0.9	2884±53

*Statistically reliable ($p<0.05$) differences between experiment and control.

Table 2. Weight of rat skeletal muscles in experiment aboard Cosmos-1667

Animal group	Weight of muscles, mg							
	soleus	gastrocnemius	plantar	long extensor of digits	quadriceps	brachial triceps	brachial biceps	brachial
Flight	122±6*	1633±45*	281±9*	152±8	2184±54	111±13*	182±3*	174±14*
Vivarium control	138±5	1850±53	343±10	166±8	2324±95	171±7	207±10	206±6
Ground-based control experiment	172±7	1863±48	325±18	174±5	2357±211	167±6	222±9	208±13
Vivarium control	169±5	1967±36	356±13	170±3	2534±53	171±10	212±10	206±8

*Statistically reliable differences, at $p<0.05$, between experiment and control.

Thus, the necropsy results and further investigations revealed that a short-term flight is not indifferent to animals, while the morphological and biochemical changes in rats following the 7-day flight are observed in the same systems and organs as following long-term flights (skeletomuscular system, hemopoietic and neuroendocrine systems, lymphoid organs, gastrointestinal tract).

However, it must be noted that we were unable to demonstrate the early signs of the changes observed in some organs in the case of 18-22-day flights. For example, in the present experiment no decline of myosin ATPase activity was detected in the myocardium (Ye. A. Nosova), although it had been observed with long-term flights [1, 2].

Distinct structural, metabolic and functional changes were observed in the skeletomuscular system. Analysis of the demonstrated changes revealed that the intensity of processes and, consequently, the rate of change were dissimilar in different muscles and skeletal bones. The greatest changes were demonstrable in the soleus muscle, while the set of changes inherent in the effects of weightlessness was the most distinct in the tibia.

The muscles presented with atrophic and dystrophic changes, and the ones primarily affected were muscle fibers with a high level of oxidative metabolism [5]. No appreciable changes were demonstrable in energy metabolism of muscles (S. M. Ivanova, O. I. Labetskaya), although accumulation of glycogen and increase in activity of phosphorylases A and B were noted in all tested muscles, and there was a decline in creatine kinase activity in the femoral quadriceps (L. M. Kurkina, T. Ye. Drozdova). The structural and metabolic changes were also associated with changes in contractility of muscles: slower contractions were observed in most tested muscles, while the soleus demonstrated a decrease in force of contraction (S. A. Skuratova, L. M. Murashko).

Histomorphometric analysis of bone structures (tibia, ileum, lumbar vertebrae; G. N. Durnova, Z. F. Sakharova, Ye. I. Ilyina-Kakuyeva) revealed signs of osteoporosis, which were the most marked in spongy matter of proximal metaphyses of the tibia. Evidently, inhibition of de novo osteogenesis is the main factor in the genesis of osteoporosis, as indicated by the decrease in number and functional activity of osteoblasts in all tested bones. The question of the role of intensification of bone resorption processes in development of osteoporosis is still unclear, since an increase in number and activity of osteoclasts was noted only in the spongiosa of tibial metaphyses. The increase in acid phosphatase activity demonstrated in the biochemical examination of these parts of bone was also indicative of activation of osteoclasts in metaphyses. Examination of mechanical properties of bones (A. V. Bakulin, V. Ye. Novikov) revealed a decrease in maximum relative deformation and increase in modulus of elasticity of bones, which is an indirect indication of the possibility of decline of their strength parameters.

Morphological studies of the hypophysis (Ye. I. Alekseyev), thyroid and parathyroid glands (G. I. Plakhuta-Plakutina) involved in humoral regulation of growth, Ca metabolism and remodling of bones were conducted in order to comprehend the genesis of the processes observed in bone. The results revealed that, after the 7-day flight, morphological signs appear of depressed function of adenohypophyseal somaotrophs that produce growth hormone and C cells of the thyroid, which produce calcitonin; this, concurrently with intensification of parathyroid function (increase in volume of parathyrocyte nuclei, number of oxyphil cells and mitoses), could cause development of osteoporosis in these animals. Thus, the systems called upon to maintain homeostasis of bone undergo a change in weightlessness in their function so as to have bone structure conform to the diminished load on bones, and the changes that develop in bone (pathological, from the standpoint of ground-based conceptions) are, in essence, a normal physiological response to absence of gravity. It must also be noted that, in spite of the presence of distinct signs of osteoporosis in spongy bone tissue and reactive changes in the thyroid and parathyroid, total calcium and parathyroid hormone content of plasma did not change, but distinct phosphatemia was observed.

Marked signs of depression of erythroid hemopoiesis in bone marrow and, particularly, the spleen were demonstrable in the hemopoietic system after the 7-day flight. The bone marrow showed a reliable decrease in erythroid elements (from 36.1% in the control to 28.2% in the experiment), and there was concurrent decrease in concentration of peripheral blood reticulocytes (N. A. Chelnaya). Virtually no sites of erythroid hemopoiesis were demonstrable in the spleen

(G. N. Durnova, Ye. V. Vorotnikova). No appreciable dynamics were observed for the above-mentioned changes during long-term flights. This indicates that physiological adaptation of the blood system to weightlessness is manifested already within the first 7 days of flight.

Immunological studies of T and B lymphocytes in bone marrow and the spleen revealed that their levels do not undergo appreciable change in the spleen, whereas the number of T lymphocytes increased in bone marrow. Evaluation of function of T lymphocytes revealed a decline in their proliferative activity and cytototoxic activity of lymphocytes that are normal killers [10]. These facts are indicative of a decline in functional capacities of the T system of immunity already at the first stage of adaptation to microgravity, and this could cause increase in rat sensitivity to bacterial and viral infections, as well as increase the risk of autoimmune processes.

Investigation of a broad spectrum of digestive enzymes (hydrolases, carbohydrases, proteases, lipases) in the stomach, intestine, salivary and submaxillary glands warrants the belief that, on the whole, the functional changes in the digestive system following a 7-day flight are in the same direction as those found after long-term flights, but they are considerably less marked [14].

It is known that the influence of weightlessness on fluid-electrolyte metabolism and renal function is among its specific effects. In our experiment, examination of different aspects of this form of metabolism in rats revealed that there was no change in electrolyte composition of blood, with the exception of phosphatemia. In addition to weight increase, the kidneys showed a decrease in potassium, sodium and magnesium content, with unchanged calcium concentration (Yu. V. Natochin, L. A. Denisova). The changes in levels of these electrolytes, particularly potassium, were also demonstrable in other organs (myocardium) and tissues (skin, muscles, bone). Direct evidence of decrease in tissue fluid content was obtained for skeletal muscles and the myocardium. Hypercreatininemia and phosphatemia can serve as indirect indicators of hypohydration and change in rat renal function, although we cannot rule out their link with changes in the skeletomuscular system as well [11].

The results of studies of the hypothalamo-hypophyseal neurosecretory system (Ye. I. Alekseyev) were also indicative of the possibility of "dumping fluid" in weightlessness; in the neurons of this system, morphological signs were observed that are inherent in diminished production of ADH vasopressin (decrease in levels of ribonucleoproteins in cytoplasm, virtually total absence of zones of synthesis of neurosecretory granules in perikaryons, 15% reduction in volume of neuronal nuclei).

With reference to the results of experiments with rats aboard biosatellites, there is constant discussion of the stressor effect of weightlessness. In this case, an answer is important to comprehension of the pathogenetic mechanisms upon which a number of changes arising in weightlessness are based. Thus, elevation of corticosterone and catecholamine levels could play some part in development of such processes as osteoporosis, inhibition of bone growth, inhibition of proliferative activity of cells, and it could cause metabolic changes, in particular, those referable to carbohydrate metabolism. A final answer to these questions can be obtained only by sacrificing animals in

weightlessness, since, as it has now been firmly established, the return to earth's gravity elicits development of acute gravity stress, and one can assess the intensity of this response in weightlessness only retrospectively, according to some criteria, primarily morphological ones.

As it was previously established [7], the most reliable indicator for a retrospective assessment is the condition of lymphoid organs and, to a lesser extent, the adrenals.

Presence of signs of involution of lymphoid tissue only in the thymus (with insignificant, 18%, decrease in its weight), without appreciable change in area of lymphoid follicles (G. N. Durnova, Ye. V. Vorotnikova) and in levels of T and B lymphocytes in the spleen, as well as absence of changes in weight or signs of hypertropy of the adrenal cortex and medulla, warrant the belief that, even at the first stage of adaptation of rats to weightlessness, there is only development of a moderate stress response, which is less strong than, for example, with hypokinesia.

Evaluation of adrenal medullary structure failed to reveal morphological signs that could be indicative of significant increase in function during the flight. Moreover, data were obtained for the flight group of rats indicative of the possibility of diminished secretion of norepinephrine in weightlessness due to the reliable decrease (by 28%) in area occupied by norepinephrine-secreting cells (N. G. Prodan).

Biochemical studies of the adrenosympathetic system using a set of criteria (blood and tissue catecholamine content, activity of enzymes of their synthesis and inactivation, condition of beta-receptors) also failed to demonstrate signs of its stimulation during the flight. On the contrary, the reliable decrease in beta-receptors of the heart and spleen is indicative of diminished sympathetic regulation in the above organs [8].

In addition to the changes listed above, which are attributable to the direct effect of weightlessnes, postflight signs of acute gravity stress were found in the rats. Analysis of its manifestations, according to morphological criteria (structure of thymus, spleen, adrenal cortex), revealed that there was a less intense response to the return to earth's gravity than following long-term flights. According to the results of biochemical studies, for example blood corticosterone content [11] and morphological composition of blood (concentration of lymphocytes and neutrophils), no such relationship was demonstrable.

Development of postflight acute stressor reactions in rats also resulted in metabolic changes in blood and tissues (such as, for example, hyperglycemia, increased antioxidant activity of blood), and accumulation of products of peroxidation of lipids was noted in the liver and muscles, whereas their concentration did not change in blood and the myocardium (N. V. Delenyan, A. A. Markin).

Investigation of reproductive function of male rats in the postflight period, which included cytolocial examination of the testes, sexual behavior, mating with intact females and evaluation of rates of development and viability of

offspring produced, failed to reveal reliable differences between the experiment and control with respect to any of the above parameters [12].

The following conclusion can be made on the basis of the results of the experiment with rats aboard Cosmos-1667 and comparing them to data obtained from long-term flights.

A set of structural, functional and metabolic changes due to the effect of weightlessness has time to develop in rats during a 7-day spaceflight. Evaluation of the demonstrated changes revealed that they reflect in essence the first stage of adaptation to weightlessness, and they are attributable primarily to the diminished functional load on different systems and the body as a whole. The rate of adaptation processes is not the same, not only in different systems and organs, but different tissues, and this is apparently caused by both the extent of decline in functional load in wieghtlessness and intensity of their inherent metabolic processes. For example, among the skeletal bones examined, the metaphyses of the tibia revealed the greatest change, whereas it was minimal in vertebrae and the soleus. Atrophic and functional changes in muscle tissue were the most distinct in muscles with a high level of oxidative metabolism. Most of the changes that appeared at the first stage progressed with increase in flight duration. This applies, in particular, to the skeletomuscular system and endocrine glands involved in hormonal regulation of growth and reshaping of bones. Some of the changes (for example, involution of the thymus, inhibition of erythroid hemopoiesis in the spleen) appear to their full extent already within 7 days, without demonstrating a tendency toward progression or recovery during long-term flights. Evaluation of the stressor effect of the first stage of adaptation to weightlessness on the basis of the results of morphological studies of lymphoid organs, adrenals and results of biochemical studies revealed that weightlessness is not a strong stress factor. Signs of dehydration and change in electrolyte concentration in some tissues, indirect biochemical parameters of change in renal function are a reflection of the changes in fluid-electrolyte metabolism. According to most tested parameters, electrolyte composition of blood remains stable. Absence of appreciable changes in biochemical parameters of blood in the presence of structureal and biochemical changes in tissues constitute a typical feature of the acute period of adaptation. This fact indicates that impairment of mechanisms of maintaining homeostasis on the level of the integral organism does not occur at the first stage of flight.

The vast experimental material obtained from this study of rats following a 7-day spaceflight can be used as the theoretical basis for analysis of the mechanisms of phenomena that develop in animals and man at the first stage of adaptation to weightlessness.

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BRAIN MORPHOGENESIS IN RATS DEVELOPING IN WEIGHTLESSNESS

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[Article by I.B. Krasnov, S. N. Olenev, I. I. Babichenko and V. S. Kesarev†]

[English abstract from source] Macroscopic and light microscopic examination of the brain of 18-day fetuses, and neonate 15-, 30-, and 100-day rats whose embryonic development from day 13 to day 18 occurred in spaceflight on Cosmos-1514 did not reveal any changes in the brain structures of the fetuses or pups of the three ages. However, the brain of the 18-day fetuses that developed in flight showed signs of insufficient tissue oxygenation, trends toward delyaed cell migration in the cortex and delayed differentiation of neurosecretory cells of the hypothalamic supraoptic nuclei. The cell differentiation rate returned to normal during continued embryogenesis after flight at 1 G.

[Text] Investigation of the effects of weightlessness on prenatal and postnatal development of the mammalian nervous system, in particular brain structures, should be considered one of the most important directions of space biology, since the result of such investigation may be the deciding factor in further exploration of space by man. There are no morphological or histochemical data in the literature concerning the effect of weightlessness on development of the mammalian brain. With respect to representatives of other classes of vertebrates, it is only in Fudulus heteroclitus fish, the embryogenesis of which occurred during spaceflight, that the brain was examined by morphological [9] and histochemical [4, 14] methods. Our objective here was to make a morphological and histochemical study of prenatal and postnatal ontogenesis of the brain of rats, the embryonic development of which occurred in weightlessness from the 13th to 18th days, during a spaceflight aboard the Cosmos-1514 biosatellite [8].

Methods

We examined the brain of 18-day fetuses and neonate rats 15, 30 and 100 days old, which developed from the 13th to 18th day of embryogesis during spaceflight aboard Cosmos-1514, as well as the brain of fetuses and rats of the same age in a ground-based synchronous experiment and vivarium control. The 18-day

flight group fetuses were decapitated 4-8 h after landing; vivarium control fetuses and those from the ground-based synchronous experiment were decapitated at the same time of day; neonate, 15-, 30- and 100-day rats were also sacrificed by decapitation. For macroscopic and histological examination, the brain of each 10- and 18-day fetus from the flight group, vivarium control and ground-based synchronous experiment, as well as the brain of each of the three 15-, 30- and 100-day rats in the flight group, vivarium control and ground-based synchronous experiment, was fixed for 24 h in a mixture of 100° ethanol--glacial acetic acid--40% formaldehyde (85:5:10). The obtained material was stored in 70° ethanol and imbedded in paraffin. Every fifth section from a series of frontal sections 10 μm in thickness was stained with chrome alum gallocyanin. For histochemical examination of the hindbrain, each of the 10- and 18-day fetuses in the flight group, vivarium control and ground-based synchronous experiment was frozen in liquid nitrogen; sections 15 μm thick were prepared in a cryostat, and histochemical techniques were used to demonstrate activity of $NAD \cdot H_2$ and $NADP \cdot H_2$ diaphorases, lactate dehydrogenase (LDH), succinate dehydrogenase (SDH), monoamine oxidase (MAO), acetylcholinesterase (ACE), alkaline (AP) and acid (AcP) phosphates. The intensity of the histochemical reactions was measured with an MTsFV-1 LOMO [Leningrad Optics and Mechanics Society] cytophotometer by the two-wave method at 535 and 595 nm for AP and the plug method in the case of LDH, using an optical probe 50 μm in diameter. Quantitative analysis of cytoarchitectonics of the neocortex of 18-day fetuses was performed by means of a tele-analyzer, using the brain of 8 fetuses from the flight group, 5 from the vivarium control and 5 from the ground-based synchronous experiment. The width of the hemisphere wall and its layers was measured in every fifth, gallocyanin-stained frontal section from the same brain, the measurements being taken in five places. This was done in a rostrocaudal direction in all parts of the cortical plate. The supraoptic nucleus and medial prominence of the hypothalamus of 18-day fetuses were submitted to electron microscopy, using 3 fetuses from the flight group, 3 from the ground-based synchronous experiment and 6 from the vivarium control, as well as the same structures and posterior lobe of the hypophysis of 3 neonate rats from the flight group, 3 from the ground-based synchronous experiment and 6 from the vivarium control; 3, 3 and 6 specimens, respectively, were used among 15-day rats and 2, 3 and 3 among 30-day animals. For electron microscopy the hypothalamus and hypophysis were fixed by immersion in 2.4% glutaraldehyde solution and in 0.08 M (fetal and neonate rat brain) or 0.1 M (15- and 30-day rat brain) phosphate buffer, pH 7.2, with additional fixing in 2% OsO_4 solution in the same buffer, and imbedded in araldite. Ultrafine sections were examined under an electron microscope.

Results and Discussion

As shown by macroscopic and visual light microscope examination, the brain of 18-day fetuses, 15-, 30- and 100-day rats of the flight group did not differ from that of fetuses and offspring of the same age in the vivarium control and ground-based synchronous experiment. It showed no sighs whatsoever of pathology, and its structures corresponded to those of fetuses and rats at the same stages of development, which had been described previously [5]. With reference to the morphological examination of brain structures receiving impulsation from the otolith system--nodulus and lateral vestibular nucleus--it must be noted that the nodulus of the cerebellar vermis is not yet formed in 18-day rat

fetuses, since formation of the sulcus separating the nodulus from the rest of the vermis occurs only on the 19th day of prenatal development [11]. Differentiation of cells of the lateral vestibular nucleus is complete by the 13th day of prenatal ontogenesis [10]. Although differentiation of types I and II hair cells in the utrical maculus of the rat fetus is complete on the 14th and 15th days, respectively, of prenatal ontogenesis [16], neuronal formation of synaptic contacts with these cells and, consequently, appearance of possibility of transmitting impulses from the otolith system to the brain occur only on the 18th day of embryogenesis [16], i.e., on the day the rat fetuses were returned to earth's gravity. Perhaps, expressly this circumstance explains the absence of morphological changes in the lateral vestibular nucleus, which receives impulsation from the otolith system, in 18-day rat fetuses that developed in weightlessness.

Mitotic activity of neuroblasts and glial elements, when measured in the region of the periventricular medulloblast matrix lining the hemisphere and striatum on the inside, in 18-day flight group fetuses did not differ with statisticaly significance from the brain of fetuses in the vivarium control and ground-based synchronous experiment. Quantitative analysis of measurements of the body of cerebral neurons undergoing the earliest differentiation--neurons of the trigeminal nerve nucleus--also failed to demonstrate statistically reliable differences between the tested groups of animals. Evidently, demonstration of an increase in number of blood capillaries in the cerebral striatum of flight group fetuses, as compared to the vivarium control and ground-based synchronous experiment (by 40 and 59%, respectively), is a sign of the brain's reaction to some inadequacy of oxygenation in fetuses that developed under spaceflight conditions aboard Cosmos-1514 (the number of capillaries per unit area of striatum sections constituted 8.15±0.53, 7.16±0.36 and 11.39±0.61 in 18-day fetuses of the vivarium control, ground-based synchronous experiment and flight group, respectively). The decrease in size and weight of the placenta, which had been established for pregnant rats of the flight group [18] and should cause a decrease in intensity of uteroplacental circulation [2], may be the cause of insufficient oxygenation of the fetal brain.

Histochemical examination of enzyme activity in hindbrain tissue of 18-day fetuses from the vivarium control and ground-based synchronous experiment revealed ACE activity in cells of the reticular formation, nerve fibers in the region of the sutura, at the fundus of the third ventricle, in nuclei of the 7th, 10th and 12th pairs of cranial nerves and descending nucleus of the trigeminal nerve. MAO activity was still very low in brain structures; it was somewhat higher in the sutural region. AcP activity is diffusely distributed in the hindbrain, and it is high only in the region ventrad to the fundus of the third ventricle. AP activity was demonstrated mainly in the endothelium of cerebral capillaries; its activity is low and diffusely distributed in nerve tissue. $NAD \cdot H_2$ diaphorase activity is rather high in all structures. This enzyme is somewhat more active in the region of the sutura and fundus of the third ventricle, nucleus of the facial nerve and descending nucleus of the trigeminal nerve. The distribution of $NADP \cdot H_2$ diaphorase activity in structures is analogous to the localization of $NAD \cdot H_2$ diaphorase, but the level of activity is lower. LDH activity is very high and diffusely distributed in hindbrain structures, whereas SDH activity is still very low.

Table 1.
Enzyme activity in rhombencephalon nerve tissue of 18-day rat fetuses (M±m)

Experimental conditions	LDH	AP
	optical density units per area of optical probe	
Vivarium control	186±7	565±28
Ground-based synchronous experim.	191±6	659±35**
Flight group	180±5	846±68*, ***

*P<0.001, as compared to vivarium control.
**P<0.05, as compared to vivarium control.
***P<0.05, as compared to ground-based synchronous experiment.

Visual analysis of histochemical preparations revealed that the level of activity and localization of the key enzymes of energy (LDH, SDH, NAD·H_2 and NADP·H_2 diaphorases) and transmitter metabolism (MAO and ACE), as well as the lysosomal enzyme AcP, in rhombencephalon structures of 18-day fetuses of the flight group did not differ from fetuses in the ground-based synchronous experiment and vivarium control. Cytophotometry also failed to demonstrate appreciable differences in LDH activity (Table 1). The results of histochemical examination warrant the assumption that there is normal development of energy and transmitter metabolism in the fetal brain during exposure of pregnant rats to weightlessness. At the same time, rat fetus development under spaceflight conditions was apparently associated with decline in intensity of metabolite transport from blood capillaries to nerve tissue. This is indicated by the visually detected decline in AP activity in the endothelium of the capillaries. Apparently, the increase in activity of the same enzyme in rhombencephalon nerve tissue of 18-day flight group fetuses is compensatory in nature (see Table 1).

Table 2. Thickness of hemisphere wall layers in 18-day rat fetuses (M±m)

Structure of wall of hemisphere	Absolute width, μm			Relative width, %		
	vivarium control	flight group	ground-based synchr. exper.	vivar. control	flight group	ground-based synchr. exper.
Marginal zone	23,0±3,2	22,7±2,1	27,5±1,2	6,6±0,9	6,4±0,6	6,6±0,3
Cortical plate	115,3±21,6	100,2±10,4	118,1±7,6	32,7±6,1	28,2±2,9	28,1±1,8
Interstitial layer	125,2±21,1	117,4±15,6	131,8±15,4	35,5±6,0	33,1±4,4	31,4±3,7
Matrix	88,9±9,2	114,4±10,9	142,4±10,4	25,2±2,6	32,2±3,1	33,9±2,5*
Hemisphere wall	352,4±48,1	354,7±35,3	419,7±25,5	100	100	100

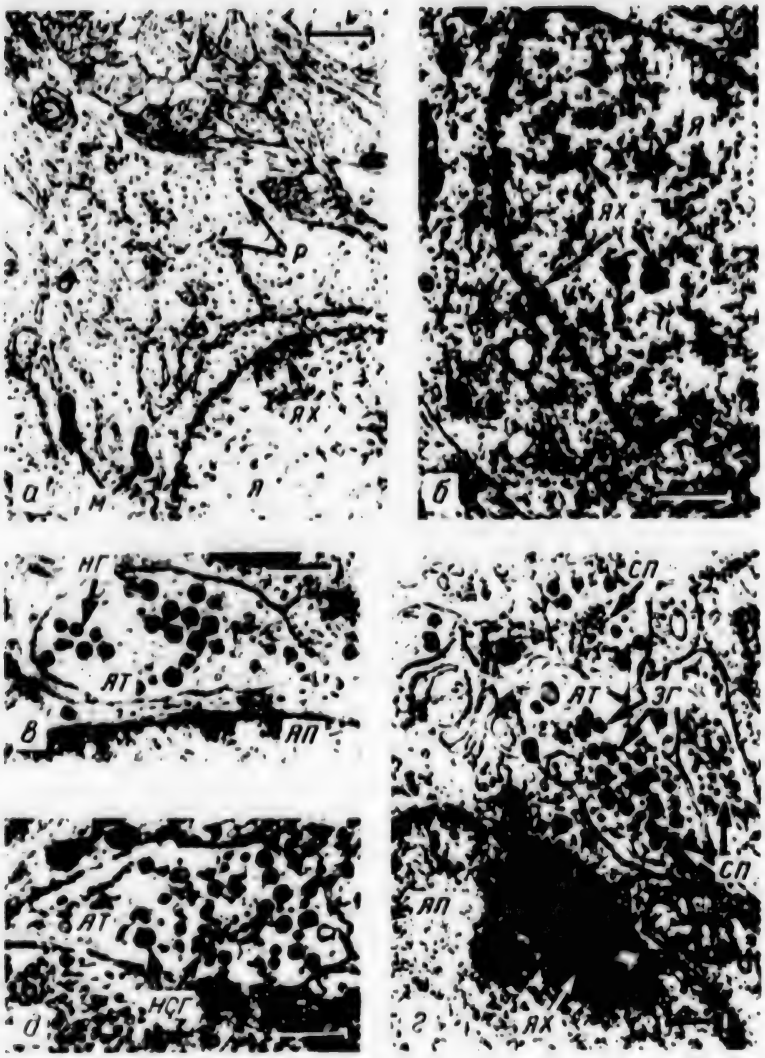
*P<0.01, in relation to vivarium control.

Qualitative analysis of cytoarchitectonics of the neocortex of 18-day rat fetuses failed to reveal and differences in extent of differentiation of neocortical structures in fetuses of the flight group, ground-based synchronous experiment and vivarium control rats. The results of quantitative analysis of cytoarchitectonics of the same structures (Table 2), as expressed in both absolute and relative units, are indicative of a tendency toward reduced width of the cortical plate and increased width of the neocortical matrix in 18-day flight group fetuses, as compared to the vivarium control; this is indicative of a

tendency toward delay in the process of cell migration from the matrix to the cortical plate. However, we cannot attribute its appearance solely to the effect of weightlessness because there is an analogous tendency in the neocortex of fetuses in the ground-based synchronous experiment.

Ultrastructural signs of retarded development of neurosecretory cells at the neuroblast stage (see Figure, *а* and *б*) are noted in the supraoptical nuclei and medial eminence of the hypothalamus of 18-day fetuses that developed in space: the neurons are characterized by a high density of distribution of nuclear chromatin (particularly heterochromatin), wide perinuclear space, narrow perikaryon; they have poorly developed canals in the rough endoplasmic reticulum and laminar complex; in the mitochondria of these cells there is inadequate development of cristae and dilatation of the space between the external and internal membrane. The ultrastructure of the neuropil is also indicative of retarded development; no fine dendrites or axonal terminals with synaptic vesicles were demonstrated, which were present along with bundles of unmyelinated fibers, dendrites and axonal hillocks and glial processes in the neuropil of 18-day fetuses of the vivarium control and ground-based synchronous experiment. In the growth cones of dendrites and axons of fetuses in the flight group, there are changes such as deformation and adherence of some vesicles and destruction of mitochondria. Along with bundles of unmyelinated fibers with intact ultrastructure, unmyelinated fibers surrounded by an enlarged extracellular space are encountered in the hypothalamus of flight group fetuses. The microtubules in such fibers are mostly dilated, with increased osmiophilia, and they are fewer in number or even wanting. No neurosecretory granules (NSG) were found in 18-day fetuses, which confirms the previously obtained data to the effect that there are no NSG in the neurons of supraoptic nuclei of rat fetuses at this stage of development [3].

Evidently, the continued prenatal development of rats following the spaceflight, at earth's gravity, normalized the rate of development of neurosecretory cells, since all of the ultrastructural elements inherent in analogous cells of vivarium control animals and those used in the ground-based synchronous experiment were present in neurosecretory cells of the supraoptical nucleus of neonate rats in the flight group. At the same time, increased chromatin density was demonstrated in the nuclei of these cells in the flight group, while the cytoplasm revealed some increase in number of microvesicles and NSG. Many fine unmyelianted fibers containing intact microtubules, mitochondria and NSG 120-160 nm in diameter were demonstrated in the medial eminence and posterior lobe of the hypophysis of neonate rats of all tested groups; in the axonal terminals of the posterior lobe of the hypophysis there were mitochondria, microvesicles 40-50 nm in diameter and large NSG 120-170 nm in diameter, which first appear in neonates [3]. In flight group neonate rats, unlike those in the vivarium control and synchronous experiment, the axon terminals revealed a dramatic increase in number of clear microvesicles 40-60 nm in diameter grouped in the center of the endings, as well as an increase in number of NSG of the granular type; this, along with the increase in nuclear chromatin density, may be indicative of increased functional activity of neurons. There is an electron-dense center (see Figure, *в* and *г*) in the axon terminals of NSG of neonate vivarium control rats. The axon terminals of neonate rats in the synchronous experiment, which contain few clear microvesicles 40-60 nm in diameter, are characterized by NSG polymorphism, there being granular, residual and disintegrating granules, as well as shadow granules (see Figure, *д*). The increase in number of clear microvesicles 40-60 nm in



Ultrastructure of bodies and axon terminals of neurosecretory neurons of hypothalamic supraoptical nuclei of 18-day fetuses and neonate rats

а,б) neurosecretory neuron of supraoptical nuclei in 18-day vivarium control and flight group fetus, respectively; magnification 9000×; scale 1 μm

в,г,д) axon terminals of neurosecretory neuron of supraoptic nuclei in posterior lobe of hypophysis in vivarium control, flight group and synchronous experiment neonate rats, respectively; magnification 17,000, 16,000 and 18,000×; scale 0.5 μm

Я) neurosecretory neuron nucleus
ЯП) pituicyte nucleus
ЯХ) nuclear chromatin
НСГ) neurosecretory granules
Р) ribosomes
АТ) axon terminal
СП) synaptic vesciles
ЗГ) granular neurosecretory granules
М) mitochondria

diameter is indicative of activation of the process of eliminating excessive calcium ions [15, 19] in terminals of the flight group neonate rats. Th s is apparently indicative of increase during the spaceflight in amount of calcium ions in neurosecretory cells which, in turn, could play an etiological role in flight group fetuses with respect to delaying differentiation of neurons [17], altering the structure of growth cones [13] and microtubules [20].

Hypertrophy and vesiculation of elements of the laminar complex, increase in number of canals in the rough endoplasmic reticulum and free ribosomes, clearing of the mitochondrial matrix and marked condensation of chromatin of the nuclear membrane are observed in pituicytes of the posterior lobe of the hypophysis of flight group neonates and those in the ground-based synchronous experiment, as compared to the vivarium control; this is indicative of increased functional activity of these cells. Considering the active role of pituicytes in eliminating neurohormones from the axon terminals, as well as the increased amount and granular structure of NSG in axon terminals of neonate rats of the flight group, it can be concluded that there is active elimination of neurosecretions in the latter. At the same time, it is difficult to offer an unequivocal answer to the question of whether this is equivalent to the reaction of neurosecretory cells of adult animals to earth's gravity following exposure to weightlessness [6, 7], since formation of the rat's neurosecretory system is completed, according to light microscopy, only by the 30th day of postnatal ontogenesis [3]. The ultrastructure of neurosecretory neurons and pituicytes in newborn rats in the ground-based experiment is also indicative of active elimination of neurosecretions; however, the structure of NSG in the terminals shows that the process of removal of neurosecretions is at a later stage and, apparently, attributable to a different cause than in the flight group of rats.

The ultrastructure of neurosecretory cells of supraoptic nuclei, axons and axon terminals of these neurons in the medial eminence of the hypothalamus and posterior lobe of the hypophysis of 15- and 30-day rats in the flight group and ground-based synchronous experiment did not differ from the findings in vivarium control animals of the same age.

The delay in differentiation of neurosecretory cells of the supraoptical nucleus is probably due to the effects of humoral factors [1]. At the same time, we cannot rule out the possibility of direct effect of weightlessness on intracellular structures of neurons that implement genetically determined processes of growth, migration and differentiation of nerve cells, in particular, on the centriole. Evidence of such an effect has already been obtained in clinostatic cultures of intervertebral ganglion neurons [12].

Thus, macroscopic and visual light-microscopic examination of the brain of 18-day fetuses, 15-, 30- and 100-day rats, the embryonic development of which took place during a spaceflight aboard Cosmos-1514 biosatellite from the 13th to 18th day, failed to demonstrate any changes whatsoever in development of structures of the brain in fetuses and rats up to the 100th day of postnatal ontogenesis. At the same time, there were signs of inadequate oxygenation of nerve tissue, a tendency toward delayed migration of cells in the cortex of the hemispheres, evidence of delayed differentiation of neurosecretory cells of hypothalamic supraoptical nuclei in the brain of 18-day fetuses that developed during spaceflight; the rates of these processes reverted to normal during continued embryogenesis after the biosatellite landed, when earth's gravity was again present.

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CIRCULATORY RESPONSE OF MALES 45-52 YEARS OF AGE TO ANTIORTHOSTATIC HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (manuscript received 20 Dec 86) pp 22-26

[Article by V. I. Sokolov, Kh. Kh. Yarullin, N. D. Vikharev, M. V. Sazonova and N. V. Degterenkova]

[English abstract from source] Regional and central circulation reactions to 30day antiorthostatic hypokinesia were investigated in 15 men, aged 45 to 52 years, with early signs of cerebrovascular and aortic atherosclerosis, neurocirculatory dystonia of the hypertensive type, and hypertensive disease of stage I. Regional and central hemodynamics of the subjects of the three groups during and immediately after exposure developed in a different manner.

[Text] Investigation of the effect of weightlessness on man is acquiring special urgency in view of expansion and intensification of research in space [3, 5, 17]. In previous model investigations [5, 16], as well as during actual spaceflights [2], it was shown that microgravity has a multifaceted effect on different physiological systems of man and, first of all, the circulatory system. However, it should be noted that investigation of hemodynamics was pursued mainly on subjects up to 40 years of age, whereas age-related distinctions of the circulatory system are discussed only in a few studies [5, 6, 20, 23]. Such investigation also acquires particular importance in view of the increase with age in incidence of cardiovascular diseases, such as atherosclerosis of cardiac vessels and the brain, essential hypertension, etc. [8], which could complicate and alter appreciably the course of the period of man's adaptation to weightlessness and the recovery period.

Methods

A study was made of central and regional hemodynamic responses of 15 men, 45 to 52 years of age, to 30-day antiorthostatic [head-down tilt] hypokinesia (-8°; HDT). The subjects were divided into two grwups: the 1st consisted of 10 men with early signs of atherosclerosis of cerebral vessels and the aorta; the 2d, of 5 men with neurocirculatory dystonia of the hypertensive type and grade I essential hypertension. The diagnoses were made following a comprehensive clinical-physiological work-up under hospital conditions.

The first group of subjects presented with polymorphic focal microsymptoms in the neurological examination, with rounding and flattening of peaks of REG [rheoencephalogram] waves, toprid responses of cerebral vessels to nitroglycerin, presence of grade I Salyus symptom ophthalmoscopically, hyperlipidemia, thickening of the ascending aorta on x-rays. Neurocirculatory dystonia of the hypertensive type was diagnosed in accordance with WHO criteria.

Examination of cerebral hemodynamics in the system of the internal carotid arteries and vertebrobasilar system was performed by the method of bipolar rheography [15] using a 4RG-1m rheograph, with recording on an 8-channel electroencephalograph. We calculated the following parameters: A (in ohms)--maximum rheogram (RG) amplitude, which reflects pulsed filling of vessels in the tested region; α/T (as percentage)--relative duration of anacrotic phase of RG, which reflects elasticity and tonus of vessels mainly of large and medium calibers [2, 13, 14, 20]; dicrotic (DCI) and diastolic (DSI) indexes, which reflect changes in tonus of small arteries and precapilaries, veins and venules, respectively [14, 15]. Since plethora of venous and venous efflux are determined mainly by the condition of veins of medium and small caliber [12], the DSI reflects not only venous return, but tonus of veins and venules [14, 15]. We also measured amplitude of the RG venous wave, which characterizes tonus of veins (mainly large ones) and efflux from them [15, 22]. Examination of cerebral hemodynamics was combined with testing of responses of the ventricular system of the brain using one-dimensional echoencephalography. The technique was described previously [10]. We calculated indexes for the third ventricle (Dvi) and medial wall of the lateral ventricle (P_{M_i}). Changes in ventricle/brain tissue ratio reflects dynamics of intracranial spinal fluid pressure.

Stroke volume of the heart (SV) and circulation volume (CV) were tested by the Kubicek [21] method of tetrapolar rheography, using an RPG2-02 rheograph with recording on a Mingograph, the data being expressed in milliliters. Arterial pressure (BP) was measured by the tachooscillographic method after N. N. Savitskiy [9]. We calculated minimum, mean dynamic, lateral, maximum and pulsed BP (in millimeters of mercury column). We also examined the hemodynamics of the right lung, liver and leg. Hemodynamic parameters were recorded before HDT, on the 2d, 6th, 17th, 27th days of hypokinesia, as well as on the 5th and 9th days of the recovery period.

The results were processed by the method of variation statistics ($p<0.05$).

Results and Discussion

Examination of cerebral circulation in the 1st group of subjects, as well as the 2d, revealed increased tonus of resistive vessels of large and small caliber; in the 1st group these changes were localized and attributable to both morphological changes in the vascular intima and extravascular factors (primarily osteochondrosis of the cervical spine), whereas in the 2d group, the increase in vascular tonus was inherent in all cerebral vessels examined and it was compensatory in the presence of high BP and, first of all, mean dynamic pressure [3]. The high tonus of intracranial veins in the 2d group of subjects (DSI = 84.5±6.1%; DSI = 66.7±7.7% in the 1st group; $p<0.05$) was associated with difficult venous efflux from the cranial cavity and dilatation of lateral ventricles of the brain (Dvi = 19.8±0.3 AU [arbitrary units]; P_{M_i} = 7.4±0.3 AU),

which is indicative of compensated form of hydrocephalus in the 2d group of subjects [2]. Higher resistance was also inherent in hepatic vessels of the 2d group of subjects.

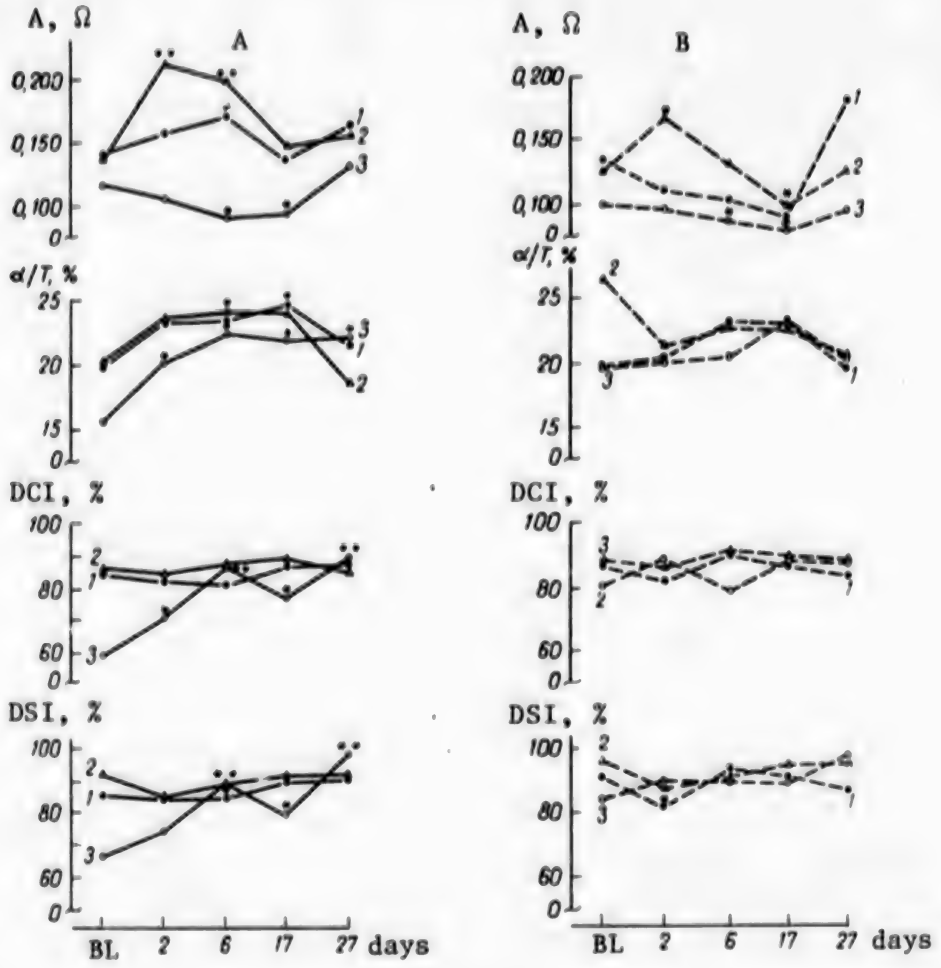

Figure 1. Dynamics of rheographic parameters of the brain in the 1st (a) and 2d (b) groups of subjects submitted to HDT

1, 2) frontomastoid lead on the right and left, respectively
3) bimastoid lead
BL) baseline

Here and in Figure 2: *P<0.05 **P<0.001

The 2d group of subjects showed increase in SV to 103.8±2.3 mℓ, which is an important compensatory factor in maintaining adequate fractions of cardiac output in individuals with this form of cardiovascular pathology.

On the 2d day of HDT, the 1st group of subjects showed an increased in pulsed filling of brain vessels in the systems of the internal carotid arteries (particularly on the left) with intensification of interhemispheric asymmetry (Figure 1a). These changes were associated with compensatory construction of large and medium caliber brain vessels, which reached a maximum on the 6th-17th day of hypokinesia (α/T increased by 24.7% on the right and 21.8% on the left),

which normalized cerebral circulation in these regions after its stabilization only by the 17th day of HDT. No reliable changes in parameter of arteriolar and venular tonus were demonstrable. The 1st group of subjects was characterized by an appreciable change in hemodynamics of the vertebrobasilar system, as manifested by 29.5% decrease in pulsed delivery of blood to vessels on the 6th-17th days of HDT. This was associated with marked increase in resistance of cerebral vessels, which was probably due not only to active vasoconstriction and presence in this group of atherosclerotic intravascular and extravascular changes in this system, but also to decrease in vasodilatation capacity of vessels [7]. An anlogous phenomenon was observed in the 2d group of subjects. On the 6th day of HDT, there was increase in tonus of arterioles and veins in the presence of difficult venous efflux in the vertebrobasilar system, which persisted up to the 17th day.

On the 6th day of HDT, such changes in cerebral hemodynamics were associated with marked dilatation of the ventricular system of the brain (Dv_i = 12.4±0.5 AU, P_{Mi} = 10.2±0.3 AU; $p<0.05$), which was probably due to elevation of spinal fluid pressure in the cranium. This could also lead to decrease in pulsed delivery of blood to cerebral vessels and elevation of arteriolar and venous tonus [2, 11].

The observed increase in pulsed delivery of blood to the carotid arteries permits compensation of hemodynamic changes in the vertebrobasilar system by means of redistribution of blood volumes in the tested regions [15].

The observed changes in cerebral circulation were associated with hypervolemia of the upper parts of the right lung and hypovolemia of the liver, which is indicative of redistribution of body fluids to the upper half of the body.

In the 1st group of subjects, we demonstrated a decline of heart rate (HR) by 14.9% on the 6th day of HDT, as compared to the baseline, and a 14% increase in HR by the 27th day (Figure 2). This was associated with 26.1% decrease in CV and 21.1% decrease in SV by the 17th day of HDT, which is due to dehydration of the body and change in fluid-electrolyte metabolism [16], as well as, to some extent, depositton of blood under HDT conditions; there was insignificant decline of BP.

In the 2d group of subjects, there were insignificantly marked hemodynamic changes in the brain during 30-day HDT. Thus, on the 2d day of hypokinesia we observed decreased pulsed delivery of blood to vessels in the system of the right carotid artery and vertebrobasilar system, which was compensated by increased pulsed filling of vessels of the left internal carotid (see Figure 1b). This was associated with insignificant dilatation of the third ventricle of the brain and difficult venous efflux from the cranium. However, absence of appreciable changes in tonus of resistive vessels, as well as cerebral veins, throughout the HDT period was inherent in the 2d group of subjects; adequate cerebral blood flow was maintained primarily by redistribution of fractions of cardiac output.

The 2d group of subjects revealed increase in pulsed and venous delivery of blood to vessels in the upper parts of the right lung and liver, which could be due not only to redistribution of fluids to the upper half of the body, but compensatory depositoin of some blood in these organs. Such changes were not

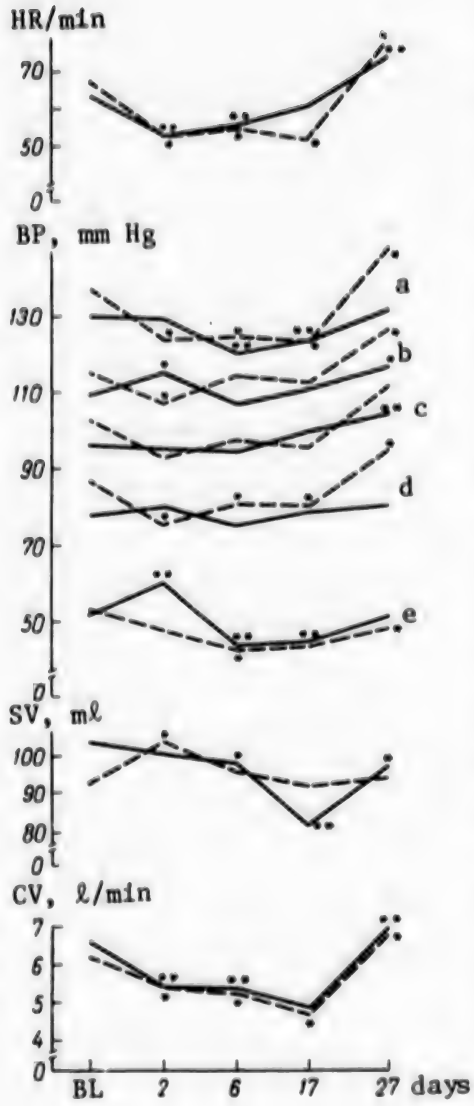

Figure 2.
Dynamics of central circulatory parameters during HDT; solid line--1st group; dash line--2d group
a-e) maximum, lateral, mean dynamic, minimum and pulse pressure, respectively
BL) baseline

observed in individuals with early signs of atherosclerosis. This can be assessed as a less significant decrease in adaptability of the 2d group of subjects in the presence of more marked decrease in capacivive properties of internal organs as a result of atherosclerotic changes in capacitive vessels in the 1st group of subjects [7].

The 2d group revealed reliable drop of maximum and lateral systolic pressure, which led to decline of pulse pressure. In this group of subjects, HR had a tendency toward decreasing, as in the 1st group. SV did not change reliably.

On the 27th day of HDT, both groups of subjects showed dramatic BP elevation, increase in vascular tonus, increase in HR by 14.0 and 11.9%, respectively. These changes probably occurred as a manifestation of the psychoemotional reaction before "getting up" after HDT, and they persisted to the end of the hypokinetic period. The hypertensive response was more marked in the 2d group.

Gradual recovery of circulatory parameters was observed in both groups on the 4th and 9th days of the recovery period. The 2d group had a slower type of recovery of hemodynamic parameters (HR, BP, pulsed delivery of blood to vessels of the brain, tonus of arterioles and venules) than the 1st group, as manifested by development of marked signs of vascular dystonia in that group, primarily referable to cerebral vessels. In the 2d group of subjects, the parameters of tonus of areterioles (DCI was 17.2% lower than the baseline in the left frontomastoid lead and 11.3% lower in the bimastoid lead) and veins (DSI was 14.4 and 16.0% lower, respectively, than the baseline), as well as BP dynamics, were indicative of incomplete recovery of both regional and central hemodynamics. Circulatory parameters reached baseline values only by the 14th-15th day, and in the 1st group the parameters did not differ reliably from the baseline as early as the 9th day of the recovery period.

Thus, the demonstrated distinctions of circulatory responses convince us that one should consider not only the age-related distinctions of responses [6], but primarily the existence of cardiovascular disease and its severity, in settling questions of professional expertise in order to predict the possible effects of microgravity on man.

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MORPHOMETRIC ANALYSIS OF RAT AORTA ENDOTHELIUM DURING LONG-TERM HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (manuscript received 4 Dec 86] pp 26-28

[Article by A. N. Gansburgskiy]

[English abstract from source] Twenty-four white rats were exposed to 30-, 60- and 100-day hypokinesia. Using the stereological technique, film preparations of their aortic endothelium were examined for the mean area of endothelial cells, nuclei and cytoplasm. Also, the content of endothelial cells showing karyopyknosis, karyolysis or binuclear structures was measured morphometrically. As compared to the matched controls, the number of cells with karyopyknosis, karyolysis and two nuclei increased significantly at every time interval studied. On hypokinesia day 30, the area of endothelial cells, nuclei and cytoplasm was greater than that in the controls. On hypokinesia days 60 and 100, the cell size was within the normal limits and the nuclear size was smaller. This led to a decrease of the nucleus-plasma ratios. Together with other factors responsible for hypercholesterinemia, the above changes in the endothelial layer may facilitate atherosclerotic lesions of the vascular wall during prolonged hypokinesia.

[Text] Structural changes in endothelium of the rat aorta, which created conditions for increased penetration of lipoproteins (LP) into the vascular wall, were demonstrated [2]. This phenomenon can be considered rather adverse, since there are concurrent changes in blood lipid and LP levels, which are a predisposing factor for atherogenesis. It has been established that metabolic disturbances instrumental in development of atherosclerosis also persist in the case of longer hypokinesia [7]. Thus far, the structure of the intima of the aorta under such conditions has not been investigated. We have studied here the condition of the rat aorta endothelium, using morphometric analysis, in the course of hypokinesia lasting up to 3 months.

Methods

Morphometric analysis was made of plane preparations of aortic endothelium from 48 white male rats with a base weight of 180-210 g. There were 24 rats each in the experimental and control groups. The experimental group of animals was

kept in individual, tight plexiglas cages. The rats were sacrificed with ether after 30, 60 and 100 days of hypokinesia (8 rats at a time). Concurrently, we took material from control animals. The thoracic aorta was fixed in Bouin fluid; film preparations of endothelium were made, they were stained with iron hematoxylin after Heidenhain. Mean area of endotheliocytes, their nuclei and cytoplasm, and nucleus-plasma ratios were determined using a stereologically ocular grid with 27 equidistant points (lens 90×, eyepiece 7×, binocular attachment 2.5×) [1]. We also kept a record of endothelial cells with pyknosis and lysis of nuclei, as well as those having two nuclei. The obtained data were processed using methods of variation statistics with special programs on an Elektronika BZ-21 microcalculator [4].

Results and Discussion

In the course of 30, 60 and 100 days of hypokinesia, destructive changes were noted in the endothelium of the aorta, as manifested by vacuolar dystrophy of cell cytoplasm, pyknosis and lysis of cell nuclei. Lymphocytes, monocytes and thrombocytes were demonstrated on the vascular intima and, occasionally, microthrombi on its surface. In addition, there was impairment of the lining of the intima, as manifested by change in shape and orientation of cells and their nuclei. This alters appreciably the cytoarchitectonics of the endothelium, intensifying heteromorphism of cell composition of the intima under hypokinetic conditions. Concurrently, we demonstrated mitotic cell division in the endothelium indicative of tissue regeneration.

Levels of some morphological parameters of rat aortic endothelium during long-term hypokinesia (M±m)

Parameter	Group	Day of hypokinesia		
		30	60	100
Karyopyknosis, %	Control	1,59±0,16	0,93±0,27	0,82±0,15
	Experiment	8,41±0,75*	4,73±0,64*	3,19±0,44*
Karyolysis, %	Control	1,14±0,37	0,66±0,21	0,99±0,40
	Experiment	10,07±0,87*	4,15±0,54*	4,76±0,36*
Binuclear cells, %	Control	1,01±0,12	0,74±0,08	0,57±0,08
	Experiment	4,55±0,50*	2,86±0,63*	1,17±0,28*
Cell area, μm^2	Control	238,10±8,46	209,33±8,22	236,20±7,40
	Experiment	332,09±24,56*	194,86±10,31	234,55±7,60
Cytoplasm area, μm^2	Control	190,67±6,42	166,52±6,66	191,90±6,30
	Experiment	258,99±16,48*	168,70±9,91	207,17±7,34
Nucleus area, μm^2	Control	47,42±3,51	42,82±1,83	44,76±4,05
	Experiment	64,0±8,63*	26,16±1,42*	27,68±2,0*
Nucleus/plasma ratios, %	Control	24,87±1,70	25,73±0,69	23,45±2,23
	Experiment	23,53±2,91	15,77±1,15*	13,45±1,11*

*$p<0.05$, as compared to matching control.

According to the results of morphometric analysis (measurements and counts are listed in the Table), throughout the experiment we demonstrated a reliable increase in relative number of endothelial cells with nuclear pyknosis and lysis. It should be noted that the most marked alterations were noted on the 30th day

of hypokinesia. The number of binuclear cells (along with enlargement of nuclei) is a morphological sign of intracellular regeneration of tissue [6]. This parameter is significantly elevated in the endothelium, with maximum rise on the 30th experimental day. Apprently, the extent of intracellular restitution is a function of severity of destructive changes in the aortic endothelim. On the 30th day of hypokinesia we demonstrated a significant increase in area of cells, cytoplasm and nuclei. Thereafter (60-100 days), the size of endotheliocytes was within the control range, but the area of nuclei diminished reliably. The latter was reflected in a decline of nucleus-plasma ratios of endotheliocytes. The dramatic increase in mean cell size recorded on the 30th day of hypokinesia is attributable to diminished density of endothelial cells. In human vessels, areas of minimal cell density are parts of the wall with maximum predisposition for atherosclerosis [5]. The decrease in size of nuclei and nucleus-plasma ratio in cells, which was demonstrated at the late stages of the experiment (60th-100th days) is a reflection of diminished functional activity of the endothelium, which is the basic tissue of the vascular wall. In addition, many cells with pyknosis and lysis of nuclei persist in the intima. These disturbances are indicative of traumatization and damage to the endothelium. It is known that factors that elicit endothelial traumatization also lead to increase in permeability of the endothelium, and they are also instrumental in processes that initiate atherogenesis [8, 9].

Thus, the changes were somewhat less marked on the 60th and 100th days than in the first month of hypokinesia. In particular, we failed to demonstrate a decrease in number of cells per unit area. At the same time, rather marked destructive changes in the nuclei persisted. This could lower significantly the capacity for regeneration of endotheliocytes. For this reason, any damage to the endothelial layer is more dangerous under hypokinetic conditions. A particularly adverse situation develops when hypokinesia is combined with other factors that cause hypercholesterolemia, since elevation of plasma level and increase in atherogenic LP fractions could elicit damage to the endothelium of great vessels [3].

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NUCLEIC ACID CONTENT OF SKELETAL MUSCLES DURING HYPOKINESIA AND IN THE RECOVERY PERIOD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (manuscript received 23 Jan 86) pp 28-31

[Article by D. Z. Shibkova and N. A. Fomin]

[English abstract from source] The concentration of nucleic acids in the gastrocnemius muscle of Wistar rats was measured during 60-day hypokinesia and 30-day recovery periods. The data obtained indicate that this hypokinetic model leads to an arrest of muscle growth and inhibition of the age-related accumulation of nucleic acids in the gastrocnemius muscle. The content of DNA and RNA genetic matrixes largely depends on the muscle activity. Normalization of the motor function results in an activation of genetic mechanisms of biosynthesis regulation, acceleration of reparative processes and recovery of muscular activity.

[Text] Immobilized animals show rapid decline of dynamic and static work capacity, as well as tonus, slower development of contractions and reduced force of muscular contraction [2, 4, 6, 7]. Skeletal muscles show dramatic tortuosity of individual fibers, disappearance of transverse and longitudinal definition, thinning of muscle fibers [3, 7, 10]. The biochemical changes, combined with morphological and functional ones, indicate that skeletal muscles are the target when motor activity is reduced [15]. However, the phenomenological findings do not reveal the intimate mechanisms of adverse effects of diminished activity on skeletal muscles. It can be assumed that the destructive changes in muscles during immobilization or diminished motor activity are based on processes of impaired biosynthesis of protein structures. The decrease in force of exogenous stimuli, which leads to impairment of repair processes effected via the DNA-RNA-protein system, may play a deciding role here. In other words, the genetic system plays a leading role in a number of processes leading to both destruction and restoration of muscular structures following hypokinesia. It is known that there is a direct link between cell function and its genetic system [8]. An increase in organ and tissue function is associated with activation of biosynthesis of nucleic acids. There are few data on change in state of nucleic metabolism in skeletal muscles during experimental hypokinesia [9, 11, 13, 15]. Further investigation of the dynamics of nucleic-acid metabolism during short- and long-term hypokinesia would provide a more distinct idea about the mechanisms of development of the hypodynamic syndrome in muscles.

Our objective here was to examine the dynamics of nucleic acid content of skeletal muscles during 60-day hypokinesia and 30-day recovery period.

Methods

This study was conducted on 140 male Wistar rats with initial weight of 180-200 g To restrict their motor activity, the animals were placed in box-cages, the size of which varied, depending on the change in animal weight. Control rats were kept under the usual vivarium conditions. Both groups were on a standard pellet diet with a supplement of vegetable oil, fish oil, fresh vegetables and water. Both experimental and control rats were weighed every 5th day. After 60-day hypokinesia, the animals were taken out of the boxes and placed in spacious cages. The animals were decapitated in a refrigerator room at a temperature of 0-4°C on the 3d, 10th, 20th, 30th and 60th days of hypokinesia, as well as 3d, 10th, 20th and 30th days of the recovery period. Their gastrocnemius was rapidly removed, tendons removed, then it was weighed and homogenized. A batch of 500 mg homogenate was taken for extraction and separation of nucleic acids by the method of G. Schmidt and S. Thanhauser [17]. A spectrophotometer was used after A. S. Spirin [14] for assaying DNA (deoxyribonucleic acid) and RNA (ribonucleic acid). The digital data were submitted to statistical processing after Student.

Results and Discussion

The dynamics of gastrocnemius weight at different stages of hypokinesia and recovery are illustrated in Figure 1. The weight of the gastrocnemiums dropped in the course of the experiment, and the lag by the end of the 1st month of hypokinesia constituted 22.1% of the baseline and 34.6% of the matching control. The second month of hypokinesia was characterized by stabilization of muscle weight in experimental animals, while the lag from control rats of the same age constituted 49.8% by the 60th day. Throughout the entire 60 days, relative weight of the gastrocnemius was below control levels.

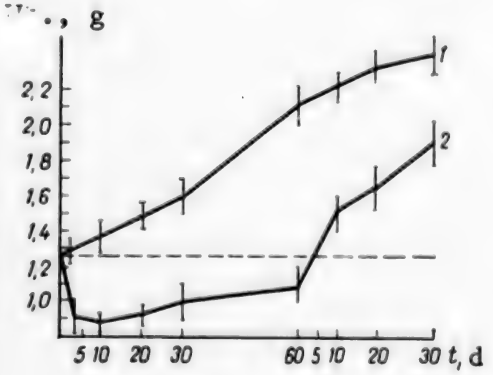

Figure 1.
Dynamics of weight of gastrocnemius; X-axis, time (days); y-axis, wt. (g)
In both figures:
1) control 2) experiment

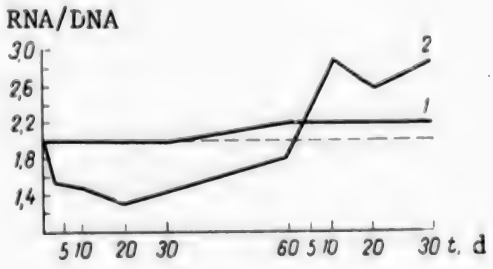

Figure 2.
Dynamics of RNA/DNA ratio in gastrocnemius; x-axis, time (d); y-axis, RNA/DNA ratio

After hypokinesia and restoration of normal motor activity, we observed a dramatic increase in animal growth and absolute weight of the tested muscle. The growth constant, calculated by the method of I. I. Shmalgauzen [16] for the gastrocnemius of experimental rats, was 4 times higher than in the control. Already by the 10th day of the recovery period the difference between weight of this muscle in control rats and those submitted to hypokinesia dropped by 22.9%. However, a difference persisted to the end of the recovery period, constituting 18%.

Concentration and amounts of nucleic acids in rat gastrocnemiums during hypokinesia for 60 days and in the recovery period

Conditions	RNA, µg/g wet tiss	RNA, µg/organ	DNA, µg/g wet tiss	DNA, µg/organ
Baseline data	1254,78±10,20	1587,30±68,90	612,59±77,90	774,93±104,00
Hypokinesia, 3 days	1273,24±49,51	1158,65±150,81	819,88±45,69	746,09±35,34
" 10 "	1280,93±65,77	1133,62±72,92	874,16±36,39	773,63±71,09
" 20 "	1276,43±88,02	1164,10±76,93	1026,08±52,57	935,78±38,62
Control after 30 "	1253,37±127,99	1888,83±38,02	619,46±39,54	933,53±9,35
Hypokinesia, 30 "	1341,11±115,99	1320,98±148,15	984,94±45,64	970,16±26,96
Control after 60 "	1284,09±128,89	2538,65±240,42	585,80±51,90	1158,13±189,92
Hypokinesia, 60 "	1495,96±67,30	1513,92±257,50	906,81±140,50	917,69±145,62
Recovery, 3 days	1677,30±131,80	1925,54±97,06	768,33±72,79	882,04±51,63
" 10 "	2028,86±110,24	2931,70±34,94	774,19±78,16	1029,06±68,19
" 20 "	1786,40±33,63	2810,00±293,82	698,78±88,86	1039,18±53,21
Control	1239,63±82,99	2751,98±207,79	552,84±53,24	1227,30±170,35
Recovery 30 "	1580,20±17,22	2875,97±240,09	614,20±26,38	1117,85±92,83

The data listed in the table characterize the concentration of nucleic acids in gastrocnemius tissue and their levels scaled to the entire muscle. It must be noted that physiological growth of control rats is consistently associated with increase in DNA and RNA content. Thus, total DNA content of the gastrocnemius increased by 49.4% and RNA by 59.9% over a 2-month period. Two-month hypokinesia inhibited appreciably the process of nucleic acid accumulation in the animals. For this reason, DNA increment constituted only 18.4% in these animals, while RNA content was below the baseline level.

Termination of hypokinesia elicited activation of nucleic acid biosynthesis. As a result, by the end of the 30th day of the recovery period DNA and RNA levels in the muscle did not differ appreciably from control values. Consequently, RNA level dropped somewhat more during hypokinesia than DNA, and this could be indicative of inhibition of the transcription process. RNA content rose faster in the recovery period than DNA, which lead to dramatic increase in RNA/DNA ratio (Figure 2). Such a ratio is inherent in rapidly growing organs, and it is indicative of faster transcription of genetic DNA matrices.

The fact that the concentration of DNA exceeded the control level by more than 50% throughout the hypokinetic period, whereas RNA did not differ appreciably from the control up to the 30th experimental day and exceeded it by 16.4% only by the 60th day merits special attention. The findings can be explained on the basis of results of electron microscopy, which was indicative of an increase in number of muscle fiber nuclei, and this is attributable to amitotic division

under hypokinetic conditions. Due to the larger size and structural distinctions of multinuclear cells during physiological and repair regeneration, they rapidly effect structural and functional replacement of dead cells [5]. The multinuclear cells should be viewed as a functional reserve of tissue that appears as a result of amitosis, which is one of the means of tissue adaptation to adverse endogenous and exogenous factors [12]. The increase in concentration of DNA per gram tissue, with decline of its level when scaled to the entire weight of the gastrocnemius, can probably be interpreted as one of the mechanisms of adaptation to hypokinesia.

On the whole, our findings warrant the conclusion that this model of hypokinesia elicits arrest of skeletal muscle growth, as well as inhibition of the age-related process of accumulation of nucleic acids in the gastrocnemiusm. The amount of genetic matrices for DNA and ribonucleic acids is markedly related to the level of muscular motor activity. Restoration of normal muscular activity leads to activation of genetic mechanisms of control of biosynthesis, faster repair processes and normalization of muscle tissue function.

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ROLE OF TESTING TOTAL GAS (O_2 AND CO_2) TENSION OF BLOOD PLASMA IN THE STUDY OF HUMAN GAS HOMEOSTASIS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (manuscript received 15 Jan 87) pp 31-41

[Article by G. Ya. Gebel, V. A. Degtyarev, V. N. Dasayev, V. N. Utkin, A. G. Kruglov, V. V. Gudenko and A. A. Lilloson]

[English abstract from source] Sixty essentially healthy subjects were examined manometrically with blood withdrawn from the coronary sinus, pulmonary artery, aorta, veins of the right kidney and the right liver lobe. Together with the traditional parameters of the gas contents and gradients of plasma, it is proposed to use tests measuring additive O_2 and CO_2 parameters. It has been demonstrated that the above organs can be discriminated using tests that are additive with respect to the gas pressure. It is emphasized that the tests proposed here, when used in addition to the traditional ones, allow identification of the gas and non-gas parameters of homeostasis as a single system of tests to assess the human body function.

[Text] Data pertaining to dynamics of blood levels of pO_2, pCO_2, $\%HbO_2$, O_2 vol.%, CO_2 vol.% and their arteriovenous gradients are used the most often in the study of systemic and organic exchange of gases [1-33].

Because of the importance of studying gas homeostasis in weightlessness or its simulation as it affects man [7, 9, 10, 17, 18], we undertook the task of expanding methodological investigative procedures and analyzing the informative value of several new tests.

We have been studying gas homeostasis (organic and systemic) since 1962 [4-11, 21, 26, 28].

On the baiss of analyisis of over 800 cases referable to man, a system of tests is offered that permits fuller comprehension of a number of conditions for control of metabolic processes involving gases (including dissociation of hemoglobin and O_2) in the following systems: organ tissues--their liquid media--blood plasma--oxyhemoglobin (organ-blood system).

Preliminary reports were made in 1984-1986 [10, 11].

The proposed test system is based on the following: 1) combining gas parameters according to their additive tags (pressure, volume). Here, we are dealing with tests that are additive in gas pressure (P): total P of gases (pO_2 and pCO_2) in blood plasma (pE, mm Hg), their gradients (ΔpE) designated as "gas functionals"; 2) determination of gradients designated as "Δp-exchange" between pO_2 level in plasma of aortal blood (pO_2AO) and total P of venous plasma gases (pEV).

In this report, we shall discuss the results of tests performed on 60 essentially healthy people (so-called "norm") breathing air.

Methods

The sounding method (under x-ray monitoring) was used to measure pressure with subjects in supine (strictly horizontal) position without loads, drawing blood samples from the coronary sinus (CS blood), pulmonary artery (AP blood), aorta (AO blood), veins (V blood), right kidney (Vr blood) and right lobe of the liver Vh blood), as well as internal right jugular (Vj blood).

An OM-2 (Radiometer) was used to measure %HbO , FEK-M unit measured hemoglobin (Hb, in g%), and ABL-1 (Radiometer) instrument for pO_2 and pCO_2 (in mm Hg).

Total P of gases in blood plasma ($pE = pO_2 + pCO_2$, in mm Hg), gradients (ΔpO_2, $\Delta \%HbO_2$, ΔpE, "Δp-exchange") between the aorta and pulmonary artery (heart-lung system), aorta and coronary sinus ("myocardium" system), aorta and renal vein ("kidney" system), aorta and internal jugular ("brain" system) were calculated on the basis of the above measurements.

The obtained data were submitted to processing by the Student-Fisher method using the t criterion. In addition, correlation analysis (we are dealing here only with conjugation signs, + and -, for reliable links without consideration of their strength) and analysis of $\%HbO_2$ in accordance with the "curves" of distribution of equilibrium between pO_2 and $\%HbO_2$ (curve of Hb and O_2 dissociation) at pCO_2 = 20-40-80 mm Hg were performed. For this purpose, we formed groups at 5% HbO_2 for V blood and 2.5% HbO_2 for AO blood. We consider the curve of distribution at pCO_2 = 40 as the basic one, and those at pCO_2 = 20 and 80 mm Hg as concomitant ones. Figures 1 and 2 single out the "zones" of AO blood pO_2 from 85 to 102.5 mm Hg.

Results and Discussion

I. The values for parameters of blood gases at the tested points and their gradients are listed in the tables and Figures 1-3.

1. Analysis of distribution of equilibrium between pO_2 and $\%HbO_2$ revealed that shifts to the left or right from the basic curve can occur in AO blood and blood of AP, renal, hepatic and jugular veins, both within the limits of concomitant zones (at $\%HbO_2$ from 85 to 70% for venous blood) and beyond the zones (for venous blood: to the left with $\%HbO_2$ over 85 and to the right, with $\%HbO_2$ under 70).

Only a right shift was demonstrated for CS blood (see Figures 1-3). It should be noted that with shifts to the left or right the pCO_2 levels do not conform to its levels at which the corresponding curves were obtained.

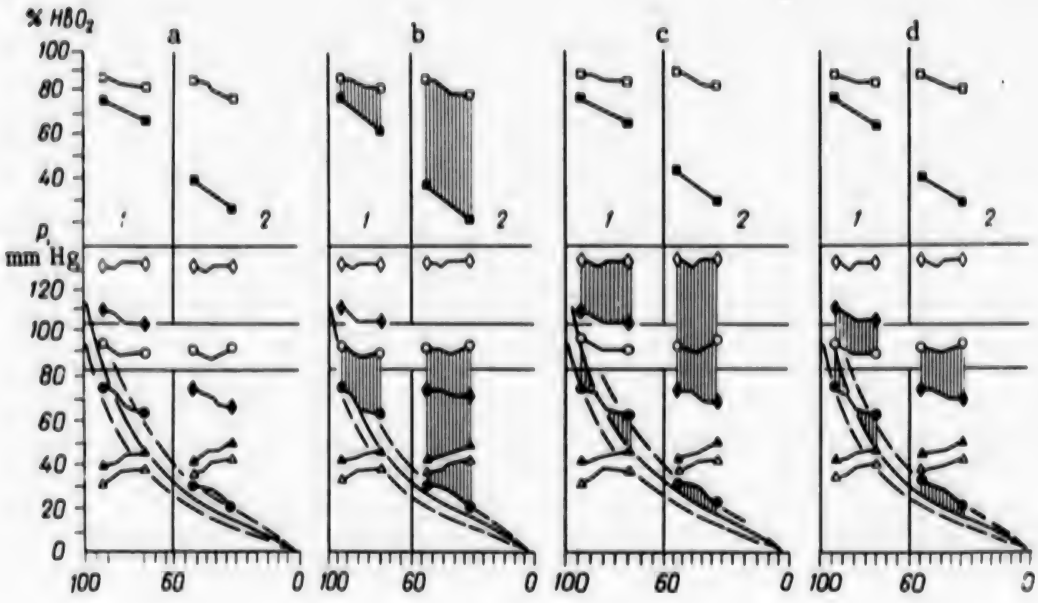

Figure 1. Distribution of gas parameters and their arteriovenous gradients in kidney and myocardium systems as a function of %HbO in V blood

a) Vr (1) and CS (2) blood gas parameters

b, c, d) gas gradients for following systems: kidney (1), myocardium (2)

b) gradients for $\%HbO_2$ and pO_2

c) gas functionals

d) Δp-exchange

Here and in Figure 2: □ and ■ -- $\%HbO_2$ of AO and V blood, respectively
○ and ● -- pO_2 of AO and V blood
◊ and ♦ -- pE of AO and V blood
△ and ▲ -- pCO_2 of AO and V blood

Table 1. Blood gas parameters (M±m)

Parameter	Blood from					
	AO	AP	Vj	Vh	CS	Vr
pO_2, mm Hg	95±2,4	54,5±2,5	50,7±2,7	51,8±2,3	26,0±1,2	70,2±2,0
pCO_2, mm Hg	39,0±2,6	40,5±2,5	45±3,0	41,2±2,0	46,5±2,0	42±2,6
$\%HbO_2$	94±1,1	80±2,2	73±2,8	75,5±2,8	39,2±2,1	82,5±3,2
pE, mm Hg	134±4,8	95±2,5	93±3,5	93±4,2	72,0±1,2	111,5±2,6

Shifts may differ in both direction (to left or right) and extent at the same time in different organs.

By virtue of these changes there is minimization of deviation of pO_2 levels in V blood, and for this reason, the same pO_2 levels can be encountered in one

organ-blood system with different $\%HbO_2$, or the same pO_2 gradients with different $\Delta\%HbO_2$ (see Figures 1-3).

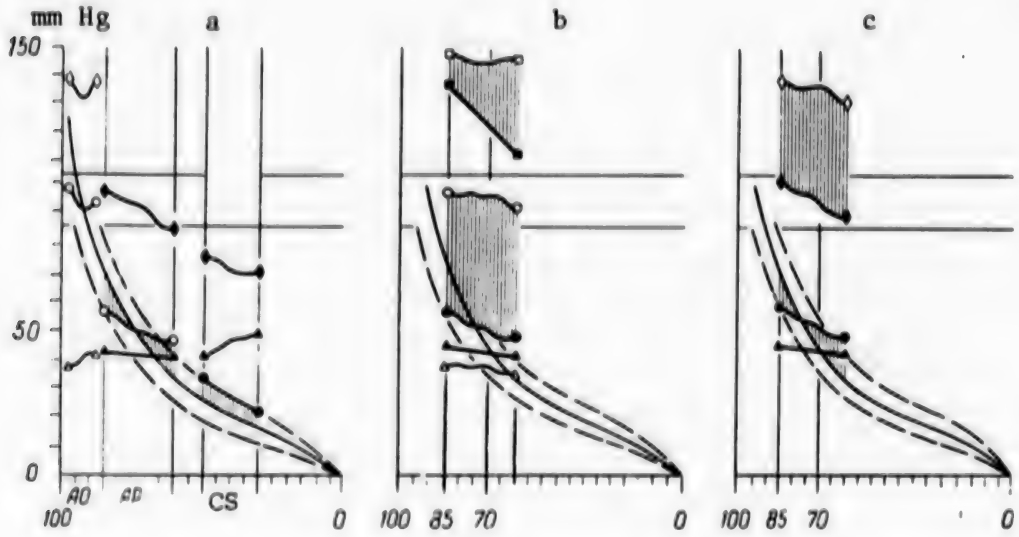

Figure 2. Gas parameters in blood during pulsating flow generated by cardiac ventricles as a function of $\%HbO_2V$ (a) and intracardiac (intercavitary) gradients of gas parameters (b and c)

Table 2. Arteriovenous differences (gradients for organ-blood systems)

Parameter	System				
	heart-lung (A-AP)	brain (A-Vj)	liver (A-Vh)	myocard. (A-CS)	kidney (A-Vr)
Δ % HbO_2	16,2±1,0	19,8±2,8	17,5±3,5	54,2±2,3	11,2±1,1
Δ pO_2, mm Hg	40,9±2,7	42,6±4,7	43,5±2,6	68,3±2,4	24,7±2,2
Δ pE, mm Hg	38,5±1,7	38,0±4,5	39,0±4,2	62,8±4,2	22,3±3,0
Δ p-exchange, mm Hg	0,0±1,2	1,1±1,5	0,0±2,3	24,5±2,8	−16,1±2,8

Correlation analysis revealed absence of reliable links: between any of the proposed tests and hemoglobin at all points (unlike tests that are additive in volume--O_2 vol.%, CO_2 vol.%, etc.) and pCO_2 of AO blood; between gas functionals and pCO_2 and pO_2 at all tested points; between total AO plasma gas P and pCO_2 at all points.

Reliable links were demonstrated for total gas P at all venous points with pO_2 (+) and pCO_2 (+) at these points (for this reason, total gas P for V blood can remain constant with changes in pCO_2, pO_2, $\%HbO_2$) and with pO_2 of AO blood (+), which is indicative of the fact that these changes occur in the same direction.

Conjugation (+) of total gas P levels at all points is a reflection of their being a function of pO_2 of AO blood.

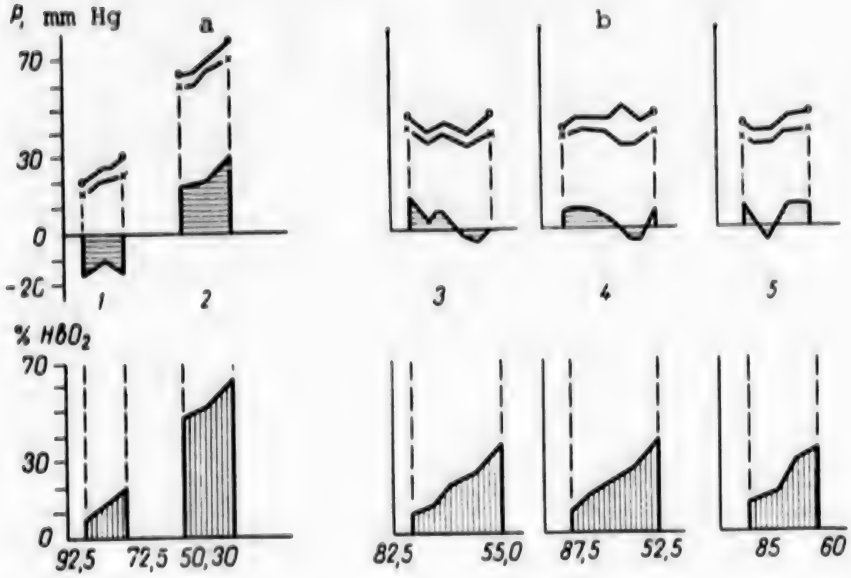

Figure 3. Distribution of arteriovenous gradients in systems with maintenance (a) and minimization (b) of deviations of Δp-exchange from zero value as a function of V blood $\%HbO_2$ levels

o--Δp0

▬--Δp-exchange

▥--Δ%Hb0

×--ΔpE

1-5--kidney, myocardium, liver, brain and heart-lung systems, respectively

Total P of CS gases is linked (+) with pO_2 of Vr blood, Δp-exchange is linked with pO_2 of AO blood (+), pO_2 (-) and pCO_2 (-) of V blood.

2. Using the proposed tests, we demonstrated qualitative differences in functional conditions of the organ-blood systems in question that cannot be detected with the usual tests.

2.1. The first group consists of organ-blood systems where *Δp-exchange deviations from zero are maintained* during eradication in them of levels of gas parameters of AO blood (maximum) and formation of gas parameters in venous blood (i.e., generation of differences between pO_2 of AO blood and pE of V blood).

This group comprises the myocardium and kidney systems.

In the myocardium system, with intermittent passage of AO blood into the microcirculatory exchange zone the following parameters are generated for a period constituting part of the cardiac cycle (see Figures 1, 3 and table): *minimum levels* of pO_2, $\%HbO_2$ and total gas P in CS blood; *maximum gas gradients* including the gas functional.

Total gas P in CS blood is *lower* than pO_2 of AO blood, and as a result Δp-exchange remains *positive in the same direction* as the other gradients of gas parameters.

Level of CS blood pO_2 corresponds to the one that is necessary and sufficient for close to maximum saturation of myocardial myoglobin. It is lower than CS blood pCO_2, i.e., the pO_2 and pCO_2 ratio in CS blood is the opposite of the one for AO blood.

These parameters are formed from the interaction of two specific proteins that are homologous many respects (myoglobin and hemoglobin), in the one hand, and various physicochemical properties, on the other (such as, for example, affinity for O_2, dependence of dissociation processes on temperature, pH, concentration of salts, rate of oxygenation, etc.).

These differences minimize the dependence of a single process (myocardial gas exchange--dissocation of AO blood HbO_2) on changes in blood biochemistry. Myoglobin can be viewed as a special type of catalyst in O_2 exchange in this process.

The levels of pO_2, $\%HbO_2$ and gas gradients in the myocardium system correspond to those demonstrated for other organs in critical situations [1, 16, 23-25] with circulatory hypoxia, and they can be designated as "hypoxic limit" criteria. Figuratively speaking, every person has his own hypoxic limit criteria in his myocardium system.

2.2. In the kidney (right) system, when there is excessive perfursion (apparently with involvement of counterflow exchange), the following parameters are generated in the microcirculatory system throughout the cardiac cycle (see Figures 1, 3 and tables): *maximum* (venous) *levels* of pO_2, $\%HbO_2$ and total gas P in Vr blood; *minimum gas gradients* including the gas functional.

Total gas P of Vr blood is *higher* than pO_2 of AO blood, as a result of which Δp-exchange is maintained as *negative and in a different direction* from the other gradients of gas parameters.

In Vr blood, pO_2 is higher than pCO_2, i.e., the pO_2 and pCO_2 ratios are analogous to those for AO blood.

In the kidney system, pO_2, $\%HbO_2$ and gas gradient levels correspond to those demonstrated in other systems under stress situations associated with the hyperkinetic syndrome in the circulatory system or impaired O_2 exchange on the organic and tissue level.

2.3. The second group consists of organ-blood systems *with minimization of deviations of* Δp*-exchange from zero value* (i.e., elimination of differences between pO_2 of AO blood and pE of V blood).

They include the heart-lung, brain and liver systems.

Analysis of mean values revealed that all of the gas parameters studied (levels and gradients) are statistically indistinguishable in these systems (see Figure 3 and Table 1).

In V blood of these systems, pO_2 and total gas P, as well as gradients for these parameters (including gas functionals) may be: greater than the corresponding "minimums" (for levels in the myocardium system, for gradients in the kidney system); lower (even with equal values for $\%HbO_2$ and $\Delta\%HbO_2$) corresponding maximums (for levels in the kidney system, for gradients in the myocardium system); same $\%HbO_2$ and $\Delta\%HbO_2$ at different levels.

The values of $\%HbO_2$ and $\Delta\%HbO_2$ may be the same as in the kidney system, but do not reach those for the myocardium system (see Figure 3).

The ratios between pO_2 and pCO_2 in AP blood, jugular and hepatic veins are not constant. The pO_2 level may be: higher than pCO_2 (as in Vr blood) with over 75% V blood $\%HbO_2$; equal to pCO_2 (± 2 mm Hg) with V blood $\%HbO_2$ at 75-65%; it may be lower than pCO_2 (as in CS blood) with $\%HbO_2$ of V blood under 65%.

The ratios of pO_2 and pCO_2, as well as the indicated range of $\%HbO_2$, can change. This depends, in particular, on left or right shifts of processes of HbO_2 dissociation. We wish to stress here the possibility of appearance and persistence of "equality" between pO_2 and pCO_2 over a rather wide range of $\%HbO_2$ for V blood.

A general condition for the function of these systems is that there must be minimization of Δp-exchange deviations from zero.

The possible Δp-exchange deviations do not normally reach this value in the myocardium system (with positive sign) or kidney system (with negative sign).

As time passes, there may be inversion of the Δp-exchange sign (+, -) with passage through zero, which could be a manifestation of the oscillatory nature of a number of functions in the human body or change in conditions of vital functionining of this system.

3. The property in common in the heart-lung, brain and liver systems is that there is a shift in blood flow with different levels of $\%HbO_2$ and pO_2.

It is known that, by virtue of the allosteric effect, a change in configuration of the protein in the hemoglobin molecule upon deoxygenation of HbO_2 alters the physicochemical properties of Hb, its affinity for O_2, dependence of the process of HbO_2 dissociation (differently on different segments of the S-shaped curve) on temperature, pH, electrolytes, a number of metabolic products (2,3-diphenyl guanine, phosphates), etc.

Mixing of flows with differences in $\%HbO_2$ and pO_2, and consequently in properties of hemoglobin as well, initiates the following conjugate processes: dissociation of Hb and O_2 with elimination of differences in $\%HbO_2$ and pO_2, generation of new levels of pO_2 and $\%HbO_2$ and equilibrium between them, pO_2 and pCO_2 ratios and their total plasma P; elimination of gradients between flows for parameters of plasma and erythrocyte media that effect cooperative regulation of processes of Hb and O_2 dissociation with establishment of new, identical levels for them, which affects affinity of Hb and O_2, and equilibrium between them.

The difference in Hb properties minimizes the dependence of these processes on biochemistry of blood, and allows for regulation of any flow via the on $\%HbO_2$ between them.

Thus, with flow mixing a process occurs that is largely analogous to the interaction between hemoglobin and myoglobin in the "myocardium" system.

It is important to stress that this process does not involve vascular membranes. In the case of concurrent transmembrane interaction with extravascular spaces in organs, prevalence of dissociation or association of Hb and O_2 depends on the pO_2 level in ambient media and change in the system of cooperative regulation, as a result of exchange of plasma elements (electrolytes, proteins, fibrinogen, etc.) with interstitial and lymphatic spaces of organs, which alters affinity of Hb and O_2.

Thus, these spaces are involved in controlling gas-exchange processes, and this is particularly important for the heart-lung and liver systems.

3.1. Systems with mixing have several specific properties.

In the brain and liver systems, minimization of Δp-exchange deviations is effected between the eliminated (pO_2 of AO blood) and generated (total V blood gases) levels.

In the brain system, mixing of AO blood with venous flow from brain tissue occurs in the chorioid plexi of the ventricles with exchange of gases with spinal fluid.

Mixing of blood of the AO and vena cava in organs of the splanchnic region ("liver" system) occurs in the hepatic sinuses during gas exchange with liver tissues.

In both systems, the process takes place throughout the cardiac cycle, with eschange with tissues and media in which pO_2 is lower than pO_2 of AO blood. Hb of venous flow is apparently a distinctive catalyst of the same process: dissociation of HbO_2 of AO blood--organic gas exchange.

In these systems, %HbO in venous flow and, therefore, gradients with AO blood depend on exchange within the systems, i.e., organs and tissues regulate dissociation of HbO_2 of AO blood on the basis of their metabolism.

3.2. The process of generating and then eliminating levels and gradients of gas parameters is a specific feature of mixing in the heart-lung system.

Generation thereof occurs in part of the cardiac cycle with flow mixing (without exchange of gases with tissues and media) in the chambers of the heart: in the right ones--blood of the venae cavae with CS blood in forming AP blood; in the left ones--blood of pulmonary and thebesian veins in forming AO blood.

Thus, the gas parameters of AO blood and AP blood, as well as their gradients between cardiac chambers (*intracardiac, intercavitary*) are produced conjugately, generally depending on myocardial metabolism at equal (mean) stroke volumes

of blood and cardiac ventricles. Blood passes from the "myocardium" system in the phase of generation of positive gradients between the coronary sinus and cardiac chambers.

Elimination of levels and gradients generated within the heart occurs within the lungs throughout the cardiac cycle, with mixing of pusating flow varying in volume converging in the pulmonary (AP blood) and bronchial (AO blood) arteries and in the alveolocapillary exchange zone of the lung (A-C zone).

This mixing in the A-C zone constitutes mixing of end products produced as a result of all metabolic processes in systemic and pulmonary circulation, and in the myocardium.

The biochemical gradients bewtween them can be viewed as one dynamic system of gradients for these end products. A change in any parameter in one of the flows causes conjugate alteration of the entire system of gradients.

Structural organization of the vascular bed (symmetrical distribution of vessels--pulmonary and bronchial arteries) provides for the common effect of biochemical (in particular, gas) composition of blood of each flow and gradients between them for all areas of the A-C zone perfused by both flows. Thus, a deviation of parameters of any flow affects lung function as a whole. This is associated with synchronization of A-C zone function as a whole with organs in systemic circulation with respect to both levels of biochemical parameters of each flow and gradients between them.

The above distinguishes the lung from other systems involving mixing ("brain," "liver"), where some organs and tissues function independently of this process, while the mixing volumes may be part of the overall perfusion volume ("brain" system).

Mixing in the A-C zone initiates the above-described processes, which take place regardless of state of alveolocapillary membranes and pO_2 levels in alveolar gas.

Hb of AO blood is a special type of catalyst in the integral process of association of Hb and O_2--gas exchange with alveolar gas.

The processes of generating and eliminating gradients of gas parameters ($\%HbO_2$, pO_2, "gas functionals," "Δp-exchange"), as well as plasma and erythrocyte factors of cooperative regulation between mixing flows, are the basis of regulation of hemodynamics, gas exchange in the A-C zone and metabolic (nongas-exchanging) function of the lungs. Through mixing processses, myocardial metabolism affects not only the hemodynamic status, but the biochemical one and gas exchange in the "heart-lung" system. These questions had been partially discussed previously with respect to the lungs, and they will be examined separately.

As a result of mixing, there is minimization of alveolocapillary gradients of pO_2, time of saturation of pulmonary vein blood to a level close to maximum, and there is change in affinity of Hb and O_2 in the A-C zone.

The processes that are initiated (upon intrapulmonary mixing of AP and AO blood) apparently affect transmembrane metabolism in the A-C zone.

Thus, there is minimization in the heart-lung system of deviations between the generated gas parameters, unlike the brain and liver systems, where this occurs between those that are eliminated and generated.

The significance of mixing of pulmonary vein blood with AP blood (shunting) and bronchial vein blood during generation of these gradients will be discussed separately. The bronchial and coronary arteries, coronary sinus and thebesian veins play the part of vascular feedback channels in the heart-lung system, synchronizing the functions of its elements according to end products of vital function of the system. Impairment of perfusion in one of them alters the function of both individual elements and the system as a whole.

II. To sum up the foregoing, the following theses must be emphasized.

1. We view total P of so-called "exchange gases" (pO_2 and pCO_2) in plasma as one of the characteristics of the overall system of metabolic products in blood. "Gas functionals" and "Δp-exchanges" constitute part of the same system of gradients of metabolic products. Their use in the study of the "norm" and variants of human pathology revealed a number of properties, described in part here.

Unlike conventional tests that reflect one process, the ones we propose take into consideration the parameters of various conjugate types of metabolism (O_2 and CO_2) occurring at the same time, expressed as a single indicator.

The levels of overall P take into consideration two parameters (O_2 and CO_2), and it is possible to investigate acts of mutual replacement.

The "Δp-exchange" considers four parameters--three levels (pCO_2 of AO blood, pO_2 and pCO_2 of V blood) and one gradient (ΔpO_2, which is always positive).

The "gas functionals" take into consideration six parameters: four levels (pO_2 and pCO_2 of AO blood; pO_2 and pCO_2 of V blood) and two gradients--positive (ΔpO_2) and negative (ΔpCO_2). The values for gas functionals, which are the algebraic sum of these gradients, are "normally" always lower than ΔpO_2.

2. All processes that minimize pO_2, pCO_2, $\%HbO_2$ and their gradients (hemodynamic, tissular, plasma, erythrocytic and others) participate in minimizing fluctuations of the tests in question. They may be manifested differently in different systems, since each "organ-bloodsystem" (particularly with flow mixing) can regulate right or left shifts in dissociation of HbO_2 in accordance with metabolism in them.

Right-left shifts minimize deviations, not only of pO_2 of V blood and ΔpO_2, but of "Δp-exchange" and "gas functionals." For this reason, they may remain constant with changes in $\Delta\%HbO_2$.

Acts of mutual replacement between pO_2 and pCO_2 are specific features of the proposed tests. Their significance is particularly manifest in the gas functionals, for which such acts of mutual replacement can occur in both AO and V blood, which is why they are "independent" of the P of different gases (see above).

The stability of the proposed tests (with changing pO_2, pCO_2, ΔpO_2) is indicative of adequacy of mutual replacement acts.

Minimization of Δp-exchange deviations for all systems is also instrumental in conjugation (+) between the levels that form it: total P of V blood gases and pO_2 of AO blood.

3. There are several properties that distinguish "Δp-exchange" from other gas gradients. Conventional gradients consider the parameters of the same process, they are always in the same direction (positive for O_2 exchange), they change only in magnitude, and they differ only quantitatively for different organs.

Unlike the conventional gas gradients, *"Δp-exchange" ones can be positive, nil, negative and their sign may change* (+, -), passing through a zero phase for some time which depends on the situations (general and organic), i.e., they can change in both magnitude and sign.

Analogous qualitative distinctions were demonstrated for a number of other parameters of homeostasis, in particular, for *hemodynamic gradients* that are generated or eliminated between cardiac chambers (*"Δp-intercavitary"*) during a cardiac cycle.

Alternation within a single cardiac cycle of positive, zero and negative values (i.e., change as a function of time), regardless of the situation, is a constant and mandatory property of "Δp-intercavitary," formed with involvement of pressure levels in the cardiac ventricles.

The duration of a gradient with a specific sign constitutes part of a cardiac cycle.

Thus, these gradients have the same properties as Δp-exchange (intracardiac) with which they are synchronized due to the common dependence on metabolic processes in the ventricular myocardium.

Interventricular, atrioventricular gradients, the gradient between the ventricles and aorta, pulmonary artery, coronary sinus are among the "Δp-intercavitary" gradients with the above-mentioned properties.

We make a distinction of two special units, between the chambers of which there is also generation or elimination of Δp-intercavitary, but with variable properties that may change as a function not only of the phase of the cardiac cycle (i.e., time) but situation. They include the following units: *aorto-pulmonary*, which comprises the trunk of the pulmonary artery and aortic bulb, which lie in the same connective tissue sheath. The touching walls of these vessels can be viewed as a separating membrane between unit chambers; *atrial*, in which the interatrial septum is also a separating membrane.

Under "normal" conditions, there may be the following gradients in these units during a cardiac cycle: "Δp-aorto-pulmonary," which are positive. They only change in magnitude at all phases (like conventional gas gradients); "Δp-left-right-atrial," which may be positive, nil or negative, i.e., they change just like Δp-intercavitary and Δp-exchange.

In a number of states, the properties of gradients in these units can change, for example, in the presence of hypertension in the left atrium--pulmonary capillaries--pulmonary artery system (with stable or low blood pressure); Δp-aorto-pulmonary gradients can acquire the properties of Δp-exchange ones, and Δp-left-right-atrium gradients can acquire the properties that are traditional in gas parameters.

All of the intracardiac gradients are formed with the participation of separating membranes (septa), among which we distinguish permanent ones (interventricular, interatrial and aorto-pulmonary) and phasic ones (generated or eliminated in the course of a cardiac cycle by pulmonary artery, aortic, mitral and tricuspid valves).

The property in common to these membranes is the capacity for deflection toward one of the chambers that they share, according to pressure gradients between them that change within a cardiac cycle.

Because of these membranes, there is phasic redistribution of volumes among unit chambers, with minimization of pressure gradients between them.

The structure of the membranes proper and changes in their properties as a function of gradient values impose limitations on this process.

Impairment of membrane function, which alters intracardiac hemodynamic conditions, affects myocardial metabolism and, consequently. conjugate formation of Δp-intercavitary and Δp-exchange gradients. Some *biochemical gradients* (positive, zero, negative) generated in the heart (*intercavitary*) and eliminated in the lungs have the properties of Δp-exchange gradients. Their sign can also change. This has been demonstrated for lactate, pyruvate, several proteins, enzymes, somatotropic hormone, insulin, fibrinogen, etc. [17, 26-29].

All of the foregoing distinguishes Δp-exchange gradients from other gas gradients, and enables us to view them as part of a broader system of gradients of homeostatic control, eliminating differences in evaluation of gas and non-gas parameters of homeostasis.

4. It is important that only Δp-exchange gradients enable us to detect systems of internal organs with qualitative differences in control of gas exchange:

a) With maintenance of deflections of Δp-exchange gradients from zero value. They include the following systems: kidney (right) and myocardium. In addition to qualitative similarity, qualitative differences have also been found in these systems with regard to levels and gradients of conventional parameters, ratio between pO_2 and pCO_2 in venous blood, sign of Δp-exchange gradients, time of generation. Both systems "normally" function conjugately (+) provided there is minimization of differences between levels (total P of CS blood gases and pO_2 of Vr blood) and gradients (Δp-exchange in the myocardium system and gas functional in the kidney system). The range of deviations between these parameters will be discussed separately.

b) With minimization of deviations of Δp-exchange gradient from zero. They include the following systems: heart-lung, brain, liver. Change in the tested gas parameters can occur for them (under "normal" conditions and those discussed

here) within the range generated in the myocardium and kidney (right) systems. Under "normal" conditions, the heart-lung system functions provided there is minimization among the following gradients that are close in value and that undergo conjugate change: Δp-exchange (intracardiac, intercavitary) generated in part of the cardiac cycle time without transmembrane gas exchange with extravascular spaces, between pO_2 in the left ventricle (AO blood) and total P of right ventricular gases (AP blood); gas functional in the alveolar gas-blood system generated throughout the cardiac cycle with participation of A-C zone vascular membranes, between total P of alveolar gases and total P of pulmonary vein blood gases.

Hemodynamic synchronization of all processes that form the above-mentioned parameters is implemented by the "atrial" and "aorto-pulmonary" units with involvement of the above membranes.

Maintaining deviations of Δp-exchange gradients in the myocardium and kidney systems is a prerequisite for minimizing their deviations in the heart-lung, brain and liver systems.

5. The proposed tests do not replace conventional ones that we consider mandatory but insufficient to assess gas homeostasis, and do not preclude the specific properties of different gases (O_2 and CO_2); rather, they supplement such tests. We believe that they permit fuller evaluation of adequacy of gas exchange in different systems of the body at AO blood pO_2 levels of 70 to 115 mm Hg. Additional tests are used when the values deviate from those indicated.

The special significance of "gas functionals," as well as the link between the proposed tests and parameters of hemodynamic and biochemical homeostasis in man under "normal" conditions, in the presence of different variants of pathology and stress states were discussed in part previously [10, 11], and will be the subject of separate consideration.

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ACID-BASE EQUILIBRIUM AND SOME RAT BLOOD PARAMETERS FOLLOWING EXPOSURE TO HYPERBARIC OXYGENATION

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[Article by V. V. Gladilov and N. A. Moyseyenko]

[English abstract from source] Acid-base equilibrium, glycolytic parameters, electrophorrtic mobility and henoglobin oxygen affinity in blood of rats exposed to hyperbaric oxygenation were measured. The animals were kept at 2026 kPa for 15, 30 or 60 min. It was found that the short-term oxygenation led to changes in acid-base equilibrium, then to biochemical changes in plasma and erythrocytes and, consequently, to a higher oxygen-binding ability of hemoglobin. The increased hemoglobin oxygen affinity was significantly stable and persisted for a certain period of time in the normal atmosphere. The experimental data demonstrated that most blood parameters taken under study varied in a different manner, depending on the time during which the animals were exposed to oxygen.

[Text] The blood system, which transports excessive oxygen to tissues and organs under the effect of hyperoxia or hyperbaric oxygenation (HBO), is one of the main systems of the body that experiences the effect of these conditions. Changes occur in blood proper that subsequently affect its biochemical and functional properties. A special role is attributed to acid-base equilibrium (ABE) of blood, a change in which in the direction of alkalosis or acidosis leads to change in permeability of red cell membranes, electrolyte composition of cells and plasma, and influences the main route of erythrocyte metabolism--glycolysis--and ultimately leads to change in one of the basic functions of blood, transport of oxygen and carbon dioxide.

Analysis of the literature does not enable us to form a distinct idea about the directions of ABE change when animals are exposed to hyperoxia and HBO [3, 5, 6]. This can be attributed to use of different modes of exposure to hyperoxia, difference in its intensity, duration and time of drawing blood for analysis. Long after exposure to HBO, many blood parameters may differ from those demonstrated at the time of oxygenation or immediately after it. We have made an attempt here to determine the time of change in ABE and a number of other red cell parameters that depend on ABE immediately after exposing animals in a pressure chamber to HBO for different periods of time.

Methods

Mixed arteriovenous blood of white rats of both sexes, weighing 250–450 g, was the material used for examination. Blood was drawn in the winter-spring period. We tested ABE with a BME-33 (Denmarkd) blood microanalyzer; and used spectrophotometry for determination of hemoglobin affinity for oxygen at partial CO_2 tension of 400 mm Hg, 37°C temperature and pH 7.2 and 7.6 of potassium-phosphate buffer solutions [2]; a nonenzyme method [8] was used to assay concentration of 2,3-diphosphoglycerate (DPG); glucose concentration, aldolase activity and reticulocyte count were determined by conventional clinical methods [11]. Heterogeneity of hemoglobin was tested by disc-electrophoresis in PAAG [expansion unknown] and a system of gels and buffer solutions No 1 after Maurer as modified for chemical polymerization [9]. Electrophoretic mobility (EPM) of different hemoglobin fractions was determined in relation to EPM of Kohlrausch's range. A hyperbaric environment was produced in a 90-ℓ hyperbaric chamber at oxygen pressure of 2026 gPa for 15, 30 and 60 min, followed by 10 min at normal air pressure. The rats were then decapitated, blood drawn and analyses performed. Control animals were kept in the same chamber in an air environment.

Results and Discussion

The results of control tests revealed that our findings as to rat blood ABE did not differ appreciably from those of other authors [3, 12]. The existence of some difference is attributable to the fact that we tested parameters of mixed blood. The other parameters were consistent with data previously reported [1, 4, 10].

Table 1. Changes in rat blood parameters as a function of duration of HBO (M±m)

Parameter	Control	Duration of HBO, min		
		15	30	60
pH	7,391±0,009 (16)	7,440±0,005* (10)	7,431±0,011 (10)	7,396±0,007 (16)
pCO_2, mm Hg	35,7±0,7 (16)	33,1±0,9* (10)	33,0±0,9* (10)	33,6±1,2 (16)
pO_2, mm Hg	55,4±2,0 (16)	54,3±1,5 (10)	56,7±2,2 (10)	58,6±2,3 (16)
BB, mmol/ℓ	44,0±0,5 (15)	47,3±0,4* (10)	44,9±1,0 (10)	43,4±1,0 (16)
BE, mmol/ℓ	−2,9±0,4 (15)	+0,2±0,6* (10)	−1,5±0,9 (10)	−3,7±0,4 (16)
SB "	22,0±0,4 (15)	24,7±0,5* (10)	23,2±0,8 (10)	21,6±0,5 (16)
AB, "	21,5±0,5 (15)	23,2±0,7 (10)	22,1±0,9 (10)	20,3±0,6 (16)
CO_2 tot., mm Hg	22,6±0,5 (15)	24,2±0,6 (10)	22,6±0,9 (10)	21,3±0,6 (16)
Glucose, mmol/ℓ	4,26±0,23 (10)	—	5,54±0,34* (11)	4,73±0,26 (10)
Aldolase, mmol/mℓ/h	0,28±0,026 (10)	—	0,11±0,024* (7)	0,26±0,050 (10)
2,3-DPG, mmol/mℓ	4,87±0,14 (10)	4,14±0,14* (11)	1,57±0,15* (7)	2,90±0,67* (10)
p50, mm Hg	35,0±0,6 (15)	35,7±1,7 (11)	33,5±0,6 (10)	29,5±1,0* (10)

Note: Number of animals given in parentheses. Asterisk indicates a statistically reliable difference from the control.

As can be seen in Tables 1 and 2, already after 15-min exposure to the oxygen atmosphere, noticeable changes occur in rat blood. This applies primarily to ABE parameters, which are indicative of development of alkalosis of mixed origin in blood. At the same time, we observed significant decrease (by 15%) in concentration of blood DPG. Evidently, reliable change in EPM of all fractions

of hemoglobin, which is indicative of conformation alterations in its molecule, is a consequence of the decreased concentration of DPG and change in medium pH.

Table 2. Change in relative EPM of rat Hb fractions in PAAG as a function of duration of HBO

Hb fraction No	Control ($n=12$)	Duration of HBO, min		
		15 ($n=9$)	30 ($n=11$)	60 ($n=13$)
1	0,52±0,002	0,51±0,003	0,54±0,003	0,55±0,002
2	0,51±0,002	0,50±0,003	0,52±0,002	0,53±0,002
3	0,47±0,002	0,46±0,005	0,46±0,002	0,47±0,002
4	0,42±0,002	0,43±0,004	0,43±0,002	0,43±0,003
5	0,33±0,002	0,35±0,003	0,37±0,002	0,35±0,003
6	0,27±0,003	0,29±0,001	0,29±0,002	0,29±0,002
7	0,22±0,002	0,23±0,004	0,24±0,002	0,24±0,002
8	—	—	0,13±0,001	0,14±0,002
9	—	—	0,08±0,003	0,08±0,002

*Hb fractions are numbered according to EPM in PAAG.

After 30-min exposure of rats to oxygen, ABE parameters, with the exception of pCO_2, did not differ from the control level. There was further decrease in DPG (by 68%). Aldolase activity diminished by 61%, while glucose concentration increased by 30%. These changes could be indicative of the fact that 30-min exposure of rats to HBO leads to inhibition of glycolysis in erythrocytes and development of a stress situation in the body. Progression of changes in red cell biochemistry caused subsequent changes in hemoglobin electrophoregrams (see Table 2): inversion of direction of EPM of fractions 1 and 2, EPM of fraction 3 remained low, whereas it increased even more in the others. There were additional, very weak minor components of hemoglobin (8 and 9) appeared, and they are apparently derived from the basic ones. Occasionally they (one or both) could also be seen in the control on the boundary of the method's resolution. However, after 30min HBO, they were distinctly demonstrable on all elecgrophoregrams. However, neither these alterations in the hemoglobin molecule nor changes in pH and DPG concentration led to modification of hemoglobin affinity for oxygen.

Exposure of rats to an oxygen atmosphere for 60 min led to normalization of most blood parameters. Reliable differences from the control were established for DPG and EPM of most hemoglobin fractions, and EPM of fractions 1 and 2 increased even more. The additional fractions also persisted on electrophoregrams. We were also impressed by the fact that it is only after such exposure that hemoglobin affinity for oxygen increased (by 16%), the curves of dissociation shifted to the left, while p50 diminished on the average by more than 5 mm Hg (see Table 1). All of the described changes occurred in red cells circulating in the vascular system and, in part, coming from the reservoir. Their concentration after 30-min HBO increased by 19% ($p<0.05$), whereas after 60 min it virtually reached baseline values. Reticulocyte concentration gradually decreased from 33.2 under normal conditions to 12.5 ‰ after 60-min HBO, i.e., by almost a factor of 3.

To calculate hemoglobin affinity for oxygen as a function of medium pH, we plotted curves of dissociation of blood hemolysates prepared in two buffer systems at pH 7.2 and 7.6. Affinity of hemoglobin for oxygen at buffer solution pH 7.6 and other conditions being equal (temperature and pCO_2) was substantially ($p<0.001$) greater, while p50 of dissociation curves (24.1 mm Hg) almost 31% lower, than p50 of the hemolysate at pH 7.2. The Bohr effect (affinity as a function of medium pH), caclulated using the formula, $\Delta \log p50/\Delta pH$, constituted a mean of -0.47, which is close to the value for rat blood, -0.52 according to other authors [12]. This parameter had a minimum of -0.38 and maximum of -0.59. Calculation of the Bohr effect was made on the basis of actual values for hemoglobin solution pH. This is related to the fact that hemoglobin can give off a certain amount of protons into the surrounding medium and, consequently, cause some acidulation of the original buffer solution: pH of the original buffer solution was 7.2, 7.6; pH of the hemolysate, 7.14 (7.0-7.20), 7.41 (7.35-7.45).

The absence if significant change in p50 of dissociation curves with exposure to HBO for 15 and 30 min indicates that brief breathing of oxygen at pressure of 2026 gPa does not affect hemoglobin affinity for oxygen. At the same time, exposure to HBO for twice the above time led to substantial increase in affinity, shifting of dissociation curves to the left and decline of p50. There was a shift in the curves for 8 out of 10 animals. In 2 animals, p50 remained unchanged.

In both control and experimental rats, when the hemoglobin solution was prepared with buffer at pH 7.6, hemoglobin affinity for oxygen increased, while p50 dropped: by 23% (p50 25.8 mm Hg) after 30-min HBO and 30% (p50 20.6 mm Hg) after 60-min HBO. However, in spite of the difference in percentile hemoglobin affinity for oxygen found at pH 7.2 and 7.6, the Bohr effect did not differ from the control. It constituted -0.48 for the former group and -0.47 for the latter. The absence of change in the Bohr effect can probably be attributed to the fact that, under HBO conditions, hemoglobin is incapable of successively being oxygenated and deoxygenated, since its molecule is oxygenated to the maximum and the Bohr effect is excluded.

Thus, the dynamics of the basic parameters of ABE, glycolysis, hemoglobin affinity for oxygen were dissimilar under our experimental conditions. The first blood changes under the effect of HBO occurred in blood ABE. After this, there was change in glycolysis parameters, which affects conformation of hemoglobin molecules, as manifested by change in EPM of its components. The dissociation curves are the last to shift. All these events develop gradually within 1 h of exposure to HBO.

The absence of changes in dissociation curves after 15 and 30 min of exposure may indicate that the effect of changing biochemical reactions in red blood cells is apparently insufficient for the dissociation curves to change their position. On the other hand, 1-h exposure to an oxygen load increases hemoglobin affinity for oxygen.

The increase in blood alkalinity at the early stage of rat oxygenation can be attributed to drop of pCO_2 and shortage of buffer bases. Since slower breathing, diminished pulmonary ventilation and decrease in heart rate were observed when

breathing oxygen already within 1-2 min, whereas in the presence of moderate hypoxia the opposite reactions prevailed [7], it should be assumed that animals that breathed oxygen for tens of minutes and then switched to air experienced hypoxia, i.e., they were subject to a hypoxic "blow" and for this reason there was change in their compensatory mechanisms of the hypoxic type.

The change in ABE in the first 15 min of HBO was a triggering mechanism for biochemical changes in red blood cells, chiefly glycolytic reactions, one of the products of which, DPG, had a strong effect on transport function of hemoglobin. However, this is not enough time to modify affinity. The same applies with respect to blood DPG level drop, which should lead to a left shift of the dissociation curves. Even dramatic decline of level of this phosphate in blood after 30-min HBO and change in conformation of hemoglobin molecules did not, according to EPM data, lead to change in protein affinity for oxygen.

According to current conceptions, alkalosis activates glycolysis and increases DPG production. Apparently, this process is different in the presence of hypoxia. The results of our experiment indicate a decline of DPG in the blood of "hyperoxic" rats with concurrent alkalization of blood. It is known that, in high concentrations, oxygen can block the key enzymes of glycolysis. This is evident in our study on the example of aldolase (see Table 1). Since the activity of this enzyme remains virtually unchanged with slight fluctuations of pH, oxygen should be considered the cause of aldolase inactivation under our experimental condtions. Hyperoxia, which inhibits glycolysis, leads to decrease in DPG production, which should lead to shifting to the left of hemoglobin dissociation curves. However, the modifying effect of DPG on hemoglobin affinity for oxygen during HBO was deferred by more than 30 min. It was manifested after 60 min, when blood phosphate levels came close to normal, while all other parameters no longer differed from normal.

Thus, relatively brief exposure of rats to HBO leads, through a set of biochemical changes in plasma and erythrocytes that occur successively after change in ABE, to alteration of hemoglobin affinity for oxygen. This modification is rather stable and persists for some time after animals start to breath air. The left shift of dissociation curves, in relation to the control level, has some significance with respect to supplying tissues at expressly this post-hypoeroxia period. This has substantial applied relevance, because cases are known in clinical practice where hypoxic signs developed in people following hyperoxia sessions. Perhaps, they developed in the presence of high hemoglobin affinity for oxygen and, as a consequence, there is difficult delivery of oxygen to tissue cells even under normal breathing conditions.

Analysis of the findings also shows that most of the tested parameters of blood change in phases, and they depend on duration of exposure of animals to oxygen. The latter could explain the contradictory nature of data in the scientific literature, since utterly opposite results can be obtained with different exposure times.

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CHANGES IN REGIONAL AND CENTRAL HEMODYNAMICS DURING SEVEN-DAY WATER IMMERSION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (manuscript received 20 Nov 86) pp 45-50

[Article by Kh. Kh. Yarullin, L. G. Simonov and S. A. Vtoryy]

[English abstract from source] Regional and central hemodynamics were assessed at bi- and tetrapolar rheography and tachooscillography during 7-day "dry" immersion and 8-day -8° head-down tilt. Blood redistribution evident from enhanced pulse filling of the brain, lungs and arms was the most pronounced on day 3-5. The onset of the blood outflow to the liver was observed on immersion day 5 due to compensatory and adaptive reactions. Lack of exercise tolerance of cardiovascular system through its insufficient training was similar in the immersion and head-down tilt for all the 6 healthy males studied (aged 41-49) despite more obvious changes in regional hemodynamics during the immersion, which recovered on its fifth day.

[Text] Studies of the effect of water immersion on the cardiovascular system are referable primarily to changes in central hemodynamics [1, 2, 6, 8, 12-15, 18]. We shall discuss here the results of studies of both central and regional hemodynamics in 6 healthy, older (41-49 years) male subjects submitted to 7 days of water immersion (WI) by the "dry" submersion method [7].

Methods

The rheoencephalogram (REG) in frontomastoid and bimastoid leads (which reflect hemodynamics in the system of the internal carotid artery and vertebrobasilar system), rheogram (RG) of the right lung, liver, leg and fingers were recorded before exposure, on the 1st, 3d, 5th and 7th days of WI and on the 5th day after it. A bipolar 4-channel 4RG-1M rheograph and 8-channel electroencephalograph (time constant 1 s) were used to record the REG and REG. Rheograph working frequency was 120 kHz and voltage 2 μV. Pulsed delivery of blood (PD) was assessed according to maximum RG amplitude measured in fractions of an ohm. We calculated relative duration of anacrotic phase of RG, α/T, %, the level of which enables us to assess tonus and elasticity of large and medium-caliber vessels. We also determined the dicrotic (DCI) and diastolic (DSI)

index of RG (as percentage), which reflect arteriolar and small artery tonus, that of venules and veins, respectively, i.e., precapillary and postcapillary resistance [9-11]. Consequently, DSI reflects primarily the state of venous efflux. Arterial pressur (BP) was measured by the tachooscillographic method. Stroke volume of the heart (SV) and minute circulation volume (CV) were determined by tetrapolar rheography (after Kubicek).

It is important that all six men participated in the test involving 8-day antiorthostatic [head-down tilt] hypokinesia (HDT). For this reason, we were able to compare the effects of WI and HDT (-8°) on regional and central hemodynamics in the same group of subjects.

Results and Discussion

On the 1st day of immersion, SV decreased from 64.4±11.1 to 45.4±11 mℓ (i.e., by 30.1%), CV dropped from 4.1±0.8 to 3.3±0.7 ℓ (by 20%), whereas on the 1st day of HDT (-8°) these parameters diminished by 12 and 17%, respectively. By the end of the 3d day of WI, SV remained 28.9% lower than the baseline value, CV was 20.3% lower ($p<0.01$). Hematocrit also changed more under the effect of WI: it rose from 42.0±1.4 to 46.8±1.2% (by 11.4%) on the 3d day of WI, and from 41.4±1.1 to 45.3±0.9% (by 9.3%) with HDT; on the 6th day the increases constituted 14.2 and 0.9%, respectively. SV was 14.7% lower than the baseline and CV was 7.8% lower on the 7th day of WI and 5th day after the latter. We observed a tendency toward elevation of diastolic and mean BP. Thus, on the 3d day of WI, BP rose from 83±4 to 87.6±3.7 and from 93±3 to 101±10 mm Hg, respectively. As we see, the decline of CV and SV occurred in the presence of some increase in peripheral vascular resistance, which had also been observed by other authors during WI [5, 7, 17]

On the 1st day of immersion, PD of right hemisphere increased by 17.8% (Figure 1), that of the left, by 32.8% and vertebrobasilar system, by 9.2% in the presence of marked increase in tonus of cerebral vessels with large and medium calibers (α/T, % by 40.3 and 54.2%). On the 3d day, PD of the right hemisphere was already 67.7% increased and on the 5th day, 73% increased, in the presence of 31% increase in α/T% and 16.8–48.7% increase in DCI, whereas on the 6th day of HDT it increased only by 32% (Figure 2). PD of the left hemisphere increased by 60.3% on the 3d day of WI, as compared to the baseline, in the presence of noticeable decrease in tonus of arterioles and veins (DCI by 13.5%, DSI by 18.8%), whereas on the 5th day it decreased and exceeded the baseline by 22.5%. On the 3d day of immersion, PD of the vertebrobasilar system exceeded the baseline by 62.3%, and there was concurrent increase in vascular tonus (α/T% by 40.3%, DCI by 42.8% and DSI by 21.1%). This greater constriction of resistive vessels, associated with increase in ratio of precapillary resistance to postcapillary resistance, leads to passage of tissue fluid into the blood stream [10, 16, 17]. The relative hypervolemia of the left hemisphere was due to active vasodilatation. On the 5th day, signs of dilatation of arterioles and small arteries also prevailed in the vertebrobasilar system (DCI on the bimastoid REG was 19.6% lower), its PD exceeded the baseline by 84%, in spite of marked compensatory increase in tonus of large vessels (α/T% by 52.3%).

As can be seen in Figure 3, on the 7th day the simultaneous compensatory constriction of large vessels, small arteries and arterioles already limited rather effectively influx of blood, and PD of the vertebrobasilar system was

12% below the baseline. PD of the hemispheres also decreased noticeably, but it exceeded the baseline by 38.6% in the system of the left internal carotid and 23% in that of the right internal carotid, in the presence of active dilatation of arterioles and veins. On the 5th day after WI, delivery of blood to all three tested regions of the brain recovered to the baseline, with normalization of tonus of precapillary and postcapillary vessels (DCI and DSI reached baseline values), and this was apparently aided by compensatory increase in tonus and elasticity of vessels with large and medium caliber (α/T% remained high).

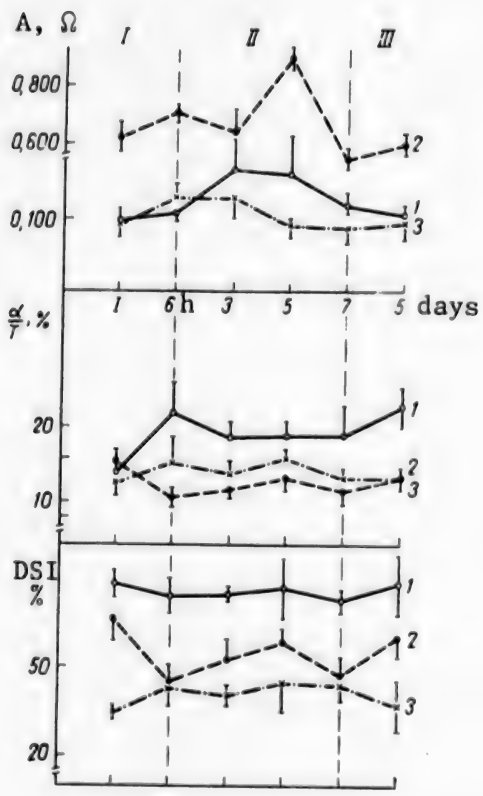

Figure 1.
Dynamics of mean values for REG parameters of right hemisphere (1), RG of right middle finger (2) and right leg before (I), during (II) and after (III) 7-day WI in 6 healthy men

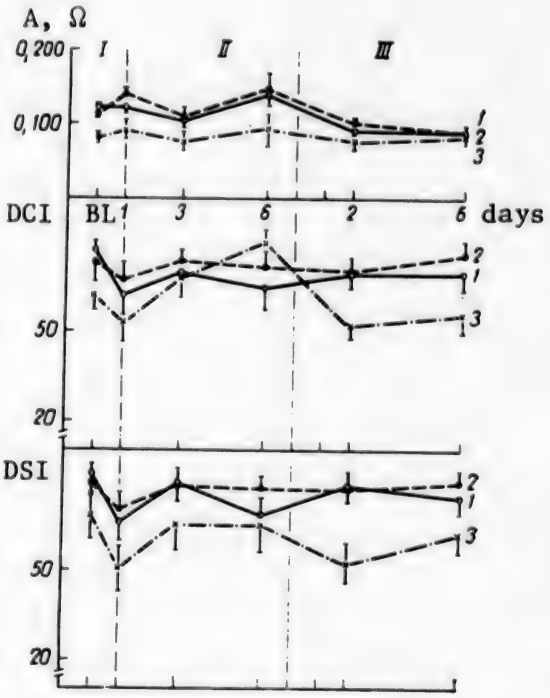

Figure 2.
Dynamics of mean values for REG parameters before (I), during (II) and after (III) 8-day HDT (-8°) in 6 healthy men

1, 2) right and left frontomastoid leads, respectively
3) bimastoid lead
BL) baseline

On the 1st day of WI, delivery of blood to the lungs increased by a mean of 59.6% (Figure 4), and in 2 subjects it increased by 173-240%. On the 3d day it decreased and was 12.7% lower than the baseline; on the 5th day it again increased and exceeded the baseline by 49.7%, whereas on the 7th day it exceeded the baseline by 36.9% in the presence of mild vasodilation reactions. On the 5th day after WI, mean PD exceeded the baseline by 85%. However, this

relative hypervolemia did not exceed the range of physiological fluctuations, in the presence of compensatory increase in tonus of arteries with large and medium calibers.

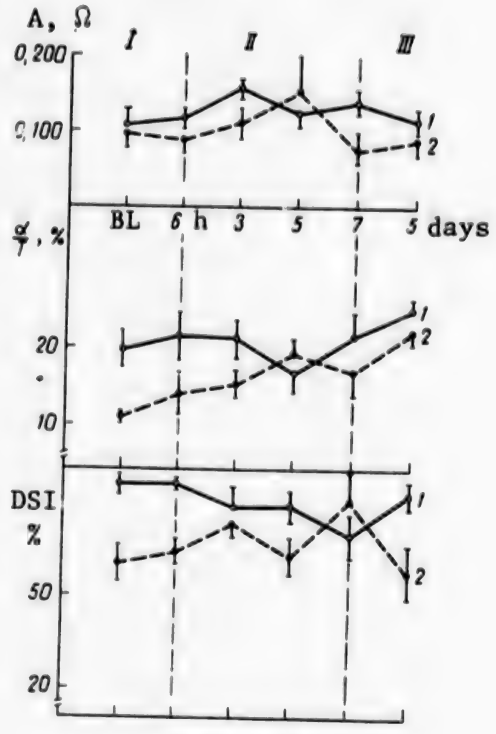

Figure 3.
Dynamics of mean REG parameters of left hemisphere (1) and in bimastoid lead (2) in 6 subjects before (I), during (II) and after (III) 7-day WI

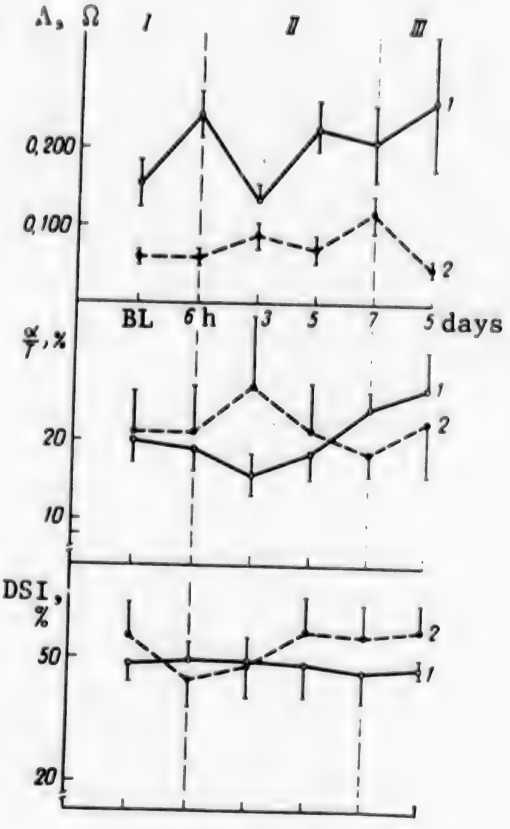

Figure 4.
Dynamics of mean RG parameters of right lung (1) and liver (2) in 6 subjects before (I), during (II) and after (III) 7-day WI

PD to liver decreased on the 1st day of WI by 21.4-34.3% in 3 subjects, and it increased by 20.1-34.9% in the other 3, in the presence of diminished tonus of arterioles and veins (i.e., mean value for DCI and DSI on rheohepatograms decreased by 26.9%). On the 3d day it increased from 0.06±0.01 to 0.092± 0.018 Ω, i.e., by 54% (see Figure 4). In one subject, whose liver (particularly the right lobe) was enlarged and palpable 3 cm below the costal arch, its PD increased by 123%, in another it increased by 81.9% and in a third, by 72.3%. On the 5th day of WI, mean PD for the liver decreased and was 23.3% greater than the baseline, in the presence of prevalence of vasoconstrictive reactions, and it was combined with increase in PD of the lungs; but in one subject (whose liver showed 1 cm enlargement at the right margin) it exceeded the baseline by 217% and in another, by 120%. On the 7th day of WI, mean PD increased even more and exceeded the baseline by 101.6% ($p<0.01$). As can be seen by comparing the dynamics of α/T,% and DSI on the rheohepatogram (see Figure 4), this hypervolemia of the liver was due to plethora of its venous

system, whereas on the 3d day, it was due to marked and active dilatation of large- and medium-caliber arteries.

Starting on the 1st day of WI, there was prevalence of vasodilatation reactions in the fingers (37.1% drop of DCI, 32.2% drop of DSI and 31.4% drop of α/T%), associated with 57.8-53.5% increase in PD on the 1st-3d days and 92.8% increase on the 5th day ($p<0.05$). On the 5th day after immersion, PD was 10.3-35.4% lower than the baseline, in the presence of a tendency toward normalization of vascular tonus (see Figure 1).

On the 5th day of WI, mean PD of the leg was 10.7% less than the baseline and on the 7th day, 12.3% less (see Figure 1), in the presence of prevalence of vasoconstrictive reactions of precapillary and postcapillary vessels (DCI increased by 33.9% and DSI by 24.4%) over dilatation of large- and medium-caliber vessels (α/T% dropped by 24.4%). Such hypovolemia of the leg was demonstrated by a number of authors during and after spaceflights [4, 10, 19]. On the 5th day after WI, mean PD of the leg reached the baseline, with normalization of vascular tonus.

According to the foregoing and Figure 1, redistribution of blood in a cranial direction was the most significant on the 3d and 5th days of WI. This was manifested by marked increase of PD of the brain, lungs and fingers. The increase in mean PD for the cerebral hemispheres and vertebrobasilar system reached 73-84% ($p<0.01$), as compared to baseline levels, whereas in the case of HDT (-8°), it did not exceed 32% in the same group of subjects. However, by the end of the WI period, cerebral hypervolemia leveled off, whereas in the case of HDT it even increased in some subjects. This warrants the belief that compensatory reactions of the cerebrovascular system are also more marked and more efficient with WI than HDT.

PD to the lungs also increased more (by 59.6%) with WI than HDT (by 14.5%), in the presence of increased tonus of arterioles and veins at first, and large- and medium-caliber arteries toward the end of immersion. These signs of pulmonary hypertension are consistent with data of other authors, who observed elevation of transmural pressure in the pulmonary artery and pressure in the right atrium during WI [12]. At the start of WI, there was marked, 34.2%, decrease in PD to the liver (versus 10% with HDT) and this, like the decline of leg PD, was related to redistribution of blood to the upper half of the body due to decline of its hydrostatic pressure [4, 10, 19]. Starting on the 3d day of WI, mean PD to the liver increased and reached a maximum on the 7th day, exceeding the baseline by 107.6%. By the end of the HDT period, however, it increased in this group of subjects by 11%. Consequently, starting on the 5th day of WI, by virtue of compensatory and adaptive reactions, there was redistribution of blood from the head, lungs and hands to the liver, and in 2 subjects an increase in its volume was also demonstrable by palpation, and was associated with unpleasant sensations in the right subcostal region. The decline of SV and CV in this period can be attributed not only to loss of plasma volume [3, 14], but to deposition of blood in the liver. Indeed, on the 3d day of WI, hematocrit rose by a mean of 11.4%, whereas CV dropped by 20.3%. Furthermore, on the 5th day after WI, in spite of normalization and even some decline of hematocrit, PD to the lungs exceeded the baseline appreciably. Here we see the obvious predominantly regional genesis of adaptive changes in

pulmonary hemodynamics. After all, the nature of hemodynamic changes depends on intensity of responses of the heart and different elements of the blood stream, particularly on the ratio between changes in resistive and capacitive vessels. As was shown above, the increase in ratio of precapillar to postcapillary resistance in the vertebrobasilar system on the 3d day of WI, which was related to greater constriction of arterioles, could be instrumental in adsorption of extravascular fluid. In some subjects, the greater increase in tonus of postcapillary vessels of the brain on the first days of WI, which lowered the above ratio, apparently enhanced filtration of fluid into tissue. By the end of the WI period, tonus parameters of small resistive and capacitive vessels of the cerebral hemispheres decreased to the same extent. Such normalization of the precapillary/postcapillary resistance ratio led to stabilization of transcapillary metabolism. This was also aided by compensatory increase in tonus of large vessels limiting influx of blood. As we see, adaptive changes in some elements of regional hemodynamics compensate for changes occurring in others. This was demonstrable just as distinctly in some of these subjects during HDT. The decrease of linear blood flow rate, demonstrable by sonodopplerography, by 15-25% in the carotid arteries on the 3d-4th day of HDT (-8°), was associated with 18-30% increase in blood flow rate in the vertebral arteries.

The passive orthostatic test performed on the 7th day of WI was associated with marked tachycardia (pulse rate rose from 70 to 113/min; before WI it rose on the average from 69 to 80/min), significant decline of PD to the hemispheres (by 42.7%) and lungs (41.9%), CV (by 32%), tonus of arteries and veins of the vertebrobasilar system (DCI and DSI on the bimastoidal REG dropped by 31.3-33.2%). These data are indicative of noticeable decrease in orthostatic stability following WI, and this was manifested by development of a presyncopic state in two subjects. Judging by the dynamics of CV and regional parameters, on the 5th day after WI there was significant improvement of orthostatic stability, and in some subjects it was even somewhat better than before WI. Already on the 2d day after WI, in spite of significant decrease of vascular tonus and PD to the vertebrobasilar system, all 6 subjects tolerated the LBNP [lower body negative pressure] test without any signs of presyncopic state. CV and PD to the lungs were moderately diminished. Perhaps, this was also caused by the greater tonus of leg veins, which was observed toward the end of WI (DSI on the leg RG was 25% higher than its level before WI). All this is indicative of adequate reserve capabilities of the cardiovascular system of healthy men 41-49 years of age.

Antiorthostatic tolerance improved considerably on the 7th day of WI, as manifested by considerably lower increment of PD to the hemispheres and cerebral vertebrobasilar system in head-down position at an angle of -30°, the increase constituting 43.7-62.8% (versus 103.7% before WI). As we see, 7-day WI reproduced all of the hemodynamic effects of being in weightlessness for 1 week.

Thus, in older healthy males, changes in regional and central hemodynamics during WI were moderate and reversible. In spite of the more marked changes in hemodynamics with 7-day WI than 8-day HDT (-8°), there was the same extent of deconditioning of the cardiovascular system according to tolerance of orthostatic tests and HDT. This may be related to greater activation of compensatory and adaptive mechanisms under the effect of WI. Evidently, immersion,

which triggers considerably more elements of adaptive mechanisms, expands their capabilities. In other words, the broader the range of normal reactions, the greater the compensatory and adaptive capabilities [5].

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SPECIFIC ORGANIC COMPOUNDS IN EXCRETA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (manuscript received 29 Oct 85) pp 50-56

[Article by M. T. Dmitriyev, A. G. Malysheva and Ye. G. Rastyannikov]

[English abstract from source] It is for the first time that chromato-mass-spectrometry was been used to examine human wastes. The data on the excretion rate of specific organic compounds can be employed to predict the content of toxic metabolites in the enclosed environment, to give their biomedical characterization, and to diagnose unfavorable changes in the body.

[Text] There is a considerable number of studies dealing with specific organic compounds in waste products [1, 2, 4, 9, 10, 13-15]. At the same time, the vast majority of data pertaining to excretion of organic substances was obtained using chemical analysis methods that are not selective enough. However, many authors have proven that it is impossible to disregard this source of atmospheric pollution. Thus, passage into air of toxic agents along with products of vital functions is one of the chief causes of atmospheric pollution in residential and public buildings [11]. Moreover, unlike this source of pollution, the adverse consequences of other sources (with migration of toxic agents from polymers, use of natural gas for cooking, etc.) can be dramatically attenuated or even eliminated (for example, by replacing gas stoves with electric ones). Release of toxic agents along with waste was also taken into consideration as a source of pollution of atmosphere in residential buildings when setting hygienic standards for population density and urban construction [5]. No doubt, this source of atmospheric pollution is quite important as well for the sealed compartments of space vehicles [3, 8]. In addition, the question of link between composition and quantity of specific organic waste and physical condition, work capacity and morbidity has not been sufficiently investigated, and this is also of interest to aerospace medicine.

Methods

A chromato-mass-spectrometer connected to a data-processing system, which consisted of a computer, display and graph plotter, was used to study human excretions. The need to use such a complicated system of chemical analysis to identify waste products was due to the fact that they have many components and

very complicated composition which cannot be identified without computerized mass spectrometry. Collection of samples and concentration of specific organic compounds from biological excreta were performed on the polymer sorbent, tenax, which is poly-2,6-diphenyl-p-phenylene oxide. This adsorbent has several advantages over the adsorption materials generally used for analogous purposes (silicagel, activated charcoal, aluminum oxide, etc.), the main ones being high thermostability and moderate adsorptivity, which permit qualitative desorption from its surface of higher hydrocarbons at 280-300°C including octadecane, chemical neutrality with regard to most organic compounds and water repellency. The latter property (specific moisture retention of tenax is 6 mg/g) is extremely important for our study, since we would otherwise encounter the very difficult task of eliminating large amounts of water, which would make analysis difficult, in studying excretions or biological fluids saturated with water vapor.

The adsorbent was placed in a sample-collecting tube of molybdenum glass, 8×200 mm in size, and fiberglass sponges were inserted at both ends to secure it. Since porous polymer sorbents absorb organic compounds from air during storage, before using them the sampler tubes were conditioned. For this purpose, the tubes were put in an adjustable electric heater heated to 280-300°C, and helium was blown through at the rate of 5-10 m/min for 24 h. Upon completion of conditioning, the samplers were sealed with fluoroplastic plugs.

Samples of excreta in gas form (in exhaled air, intestinal gases, etc.) were collected into fluoroplastic sacks up to 10 ℓ in size. The sacks with samples were connected to adsorption tubes and their outlets, to a vacuum pump. The pumping rate was 200 mℓ/min and volumes of tested air with excreta constituted 5-10 ℓ. The tests were conducted on 56 healthy subjects.

Gas extraction was used to remove specific organic compounds from biological fluids (urine, saliva, washings, etc.) and feces. Liquid excreta (or aqueous solutions thereof, or suspensions) were placed in tapered glass flasks with inlet and outlet connections to pump helium through. The inlet tube reached the bottom of the flask and had a gas diffuser at the end in the form of a sphere with fine holes. Adsorption tubes with tenax were connected to the outlet tubes. Gas (highly pure helium) bubbled through the fluid caused desorption of specific organic substances from fluid and their subsequent absorption on the surface of the adsorbent as a reuslt of continuous gas extraction.

Perspiration was collected from the skin surface with cotton sponges; the specimens were weighed and placed in a tube, to the outlet end of which we also connected adsorption tubes with tenax through a silicon rubber hose. Concentrated organic compounds were extracted from the surface of the adsorbent by means of thermal desorption in a narrow metal capillary cooled with liquid nitrogen. The thermal desorption process was conducted at a temperature of 280-300°C.

Analysis of biological excreta was performed under the following conditions. For gas-chromatographic separation we used a glass capillary chromaographic column 0.3 mm in diameter and 38 m in length, which was treated with SE-30 silicon. For the first 5 min, chromatographic separation was performed at room

temperature. Then the column temperature was programmed at the rate of 5°C/min to 150°C. Identification of the compounds recorded on the chromatogram was made using a catalogue of mass spectra [12] and computer file of spectra. The chief advantage of computerized chromato-mass spectrometry for analysis, as compared to others, is unequivocal identification of compounds [7], which is particularly important when analyzing such complicated mixtures as products of vital functions, which consist of many hundreds of components.

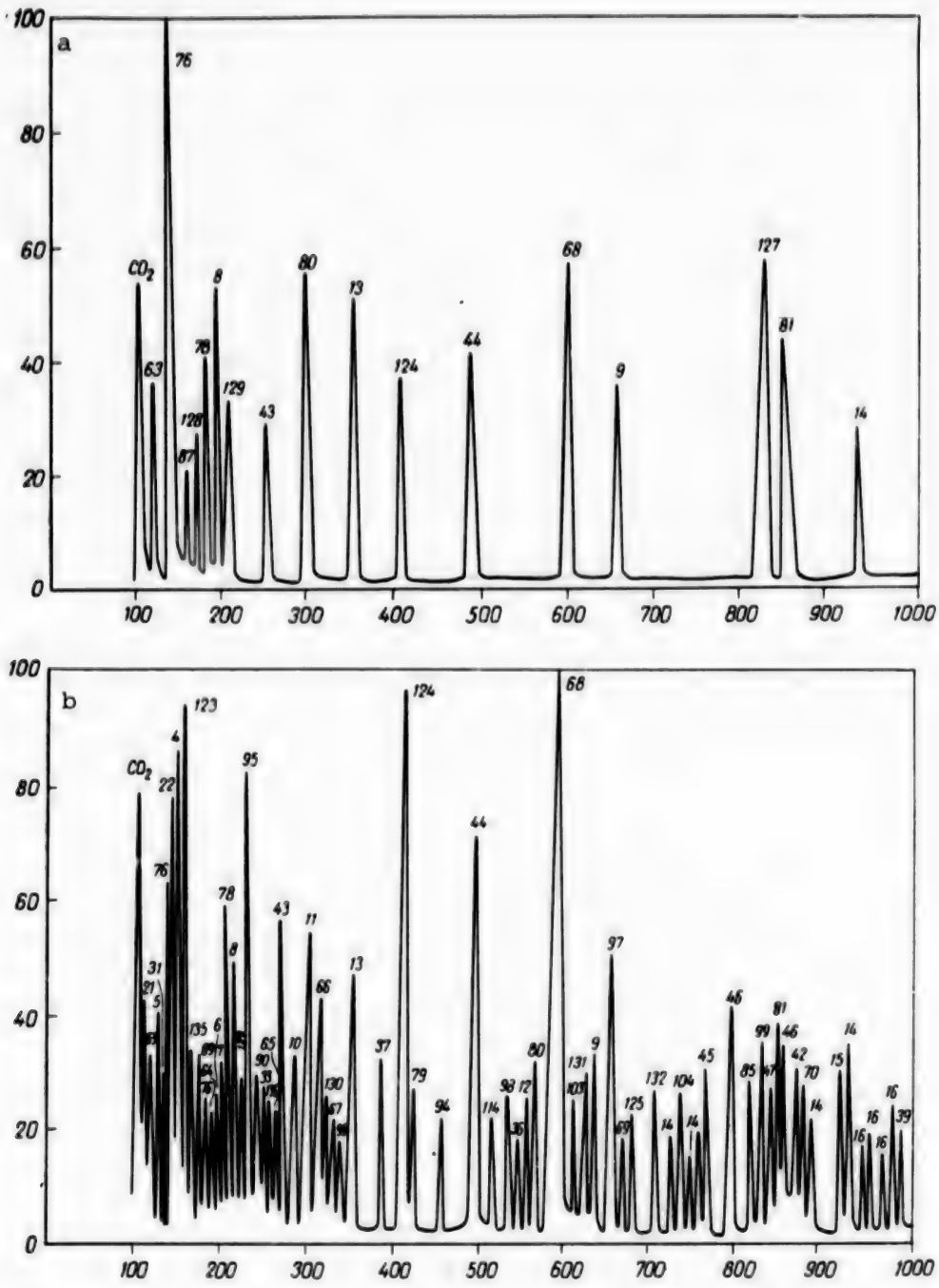
Chromato-mass spectrometry was performed of specific organic compounds excreted by the human body.

Results and Discussion

As an example, the figure illustrates segments of computerized chromatograms of gases in urine and feces. Computer identification of mass spectra in excreta established the presence of such specific, toxic, organic compounds as isoprene, methyl mercaptan, ethyl mercaptan, 2,3,4-trithiopentane, chlorobenzene, methyl chloride, trichloroethylene, tetrachloroethylene, acetonitrile, pyrrolidine, methylpiperazine, n-methylpyrrole, 1,4-dioxane, diphenyl ether, heptanal, decanal, furfural, benzaldehyde, 2,4-hexadienal, naphthalene and its derivatives, 2-butanone, 4-hepatonone and 2-decanone.

The table lists data on intensity of excretion into the air environment of the main specific organic compounds with various excreta. As can be seen from this table, the identified substances are referable to various classes of chemical compounds--saturated, unsaturated, napthenic, aromatic hydrocarbons, oxygen-containing compounds (aldehydes, ketones, alcohols, ethers), nitrogen-, chlorine-, fulfur-containing, etc. It is of substantial interest to note that significant amounts of specific oxygen-containing compounds were identified in excreta: aldehydes (primarily acetaldehyde, hexanal, pentanal, octanal, heptanal, nonanal, benzaldehyde), ketones (methylethyl ketone, acetone, 2-butanone, 4-heptanone), alcohols (ethanol, methanol, isopropanol), ethers (ethyl acetate, butyl acetate, 1,4-dioxane), as well as formic acid, p-cresol and phenol. Among the sulfur-containing compounds, dimethyl disulfide is represented in appreciable concentrations; among chlorine-containing compounds, chloroform, methyl chloride; nitrogen-containing--methylamine, isopropylamine; aromatic hydrocarbons--benzene, toluene, xylene; unsaturated hydrocarbons--isoprene, ethylene, butilene; saturated--methane, ethane, propane.

The obtained data on intensity of excretion of specific organic compounds can be used to predict levels of toxic excretions in the atmosphere of sealed compartments and to furnish a biomedical evaluation thereof. Concentrations of excreta as toxic agents in the atmosphere can be calculated on the basis of the volume of sealed rooms, number of people, time spent in such rooms, extent of purification and frequency of recirculation. Considering the permissible levels of substances in air when each is evaluated separately by methods of quantitative toxicology, one can determine the overall indicators of atmospheric pollution and, using them, one can assess the adverse effects on man, decline of work capacity and possible morbidity, depending on concrete conditions. Excretion of specific substances can also be used to detect adverse physical conditions [6].



Segments of computerized chromatograms of specific organic compounds excreted into the air environment in urine (a) and feces (b)

X-axis: mass spectrum number; y-axis: relative intensity of chromatographic peak (maximum arbitrarily set at 100). The names of identified substances corresponding to peak numbers on the chromatogram are listed in the table.

Excretion into the air environment of specific organic compounds*

Substance	Excretion, μg/h				
	in exhaled air	sweat	urine	feces	total
Saturated hydrocarbons					
Methane	$2,52 \cdot 10^4$	$1,24 \cdot 10^4$	$9,87 \cdot 10^3$	$2,15 \cdot 10^5$	$2,62 \cdot 10^5$
Ethane	$1,34 \cdot 10^4$	$6,31 \cdot 10^3$	$4,78 \cdot 10^3$	$9,26 \cdot 10^4$	$1,17 \cdot 10^5$
Propane	$1,17 \cdot 10^4$	$4,38 \cdot 10^3$	$2,64 \cdot 10^3$	$7,53 \cdot 10^4$	$9,40 \cdot 10^4$
Pentane	$2,46 \cdot 10^3$	$1,17 \cdot 10^3$	$3,03 \cdot 10^3$	$2,05 \cdot 10^4$	$2,72 \cdot 10^4$
Isopentane	$2,13 \cdot 10^3$	$1,08 \cdot 10^3$	$2,66 \cdot 10^3$	$1,81 \cdot 10^4$	$3,30 \cdot 10^4$
2-Methylpentane	$3,22 \cdot 10^3$	$2,68 \cdot 10^3$	$1,86 \cdot 10^3$	$2,95 \cdot 10^3$	$5,40 \cdot 10^3$
3-Methylpentane	$3,04 \cdot 10^3$	$2,14 \cdot 10^3$	$1,26 \cdot 10^3$	$2,61 \cdot 10^3$	$3,25 \cdot 10^3$
Hexane	$2,62 \cdot 10^3$	$1,54 \cdot 10^3$	$8,31 \cdot 10^3$	$1,67 \cdot 10^3$	$2,92 \cdot 10^3$
Octane	$2,34 \cdot 10^3$	$1,26 \cdot 10^3$	$6,72 \cdot 10^2$	$1,58 \cdot 10^3$	$2,61 \cdot 10^3$
2-Methylhexane	$2,29 \cdot 10^3$	$1,61 \cdot 10^3$	$5,86 \cdot 10^2$	$1,43 \cdot 10^3$	$2,41 \cdot 10^3$
3-Methylhexane	$2,56 \cdot 10^3$	$1,73 \cdot 10^3$	$5,99 \cdot 10^2$	$1,37 \cdot 10^3$	$2,40 \cdot 10^3$
2,2,5-Trimethylhexane	$2,35 \cdot 10^3$	$1,24 \cdot 10^3$	$4,61 \cdot 10^2$	$1,24 \cdot 10^3$	$2,06 \cdot 10^3$
Heptane	$2,21 \cdot 10^3$	$1,43 \cdot 10^3$	$3,74 \cdot 10^2$	$1,15 \cdot 10^3$	$1,89 \cdot 10^3$
Nonane & isomers	$1,26 \cdot 10^3$	90,2	$3,38 \cdot 10^2$	$1,07 \cdot 10^3$	$1,84 \cdot 10^3$
2,5,5-Trimethylheptane	$1,23 \cdot 10^3$	80,5	$2,95 \cdot 10^2$	$9,58 \cdot 10^2$	$1,46 \cdot 10^3$
Decane & isomers	$1,19 \cdot 10^3$	70,1	$2,41 \cdot 10^2$	$7,84 \cdot 10^2$	$1,21 \cdot 10^3$
Undecane & isomers	$1,07 \cdot 10^3$	74,2	$2,05 \cdot 10^2$	$5,63 \cdot 10^2$	$9,49 \cdot 10^2$
Dodecane & isomers	$1,01 \cdot 10^3$	65,4	$1,93 \cdot 10^2$	$4,37 \cdot 10^2$	$9,63 \cdot 10^2$
Tridecane & isomers	94,6	52,1	$1,57 \cdot 10^2$	$2,46 \cdot 10^2$	$5,50 \cdot 10^2$
Unsaturated hydrocarbons					
Ethylene	$2,24 \cdot 10^3$	$1,56 \cdot 10^3$	$1,27 \cdot 10^3$	$3,81 \cdot 10^4$	$3,98 \cdot 10^4$
Butylene	$1,14 \cdot 10^3$	94,3	$6,64 \cdot 10^2$	$5,34 \cdot 10^3$	$6,21 \cdot 10^3$
Isoprene	$1,35 \cdot 10^3$	$8,75 \cdot 10^2$	$6,56 \cdot 10^3$	$1,64 \cdot 10^4$	$2,52 \cdot 10^4$
Heptene-1	87,3	65,4	$5,12 \cdot 10^2$	$1,21 \cdot 10^3$	$1,87 \cdot 10^3$
Decene-1	66,4	60,7	$4,63 \cdot 10^2$	$1,03 \cdot 10^3$	$1,62 \cdot 10^3$
Diisoamylene	21,0	11,4	$3,59 \cdot 10^2$	$9,14 \cdot 10^2$	$1,31 \cdot 10^3$
Undecene-1	29,1	17,4	$3,01 \cdot 10^2$	$7,85 \cdot 10^2$	$1,13 \cdot 10^3$
Dodecene-1	20,4	18,9	$2,68 \cdot 10^2$	$5,63 \cdot 10^2$	$9,10 \cdot 10^2$
Tridecene-1	17,5	16,0	$1,43 \cdot 10^2$	$2,73 \cdot 10^2$	$4,14 \cdot 10^2$
4-Methyloctadiene-1,7	15,4	15,1	94,5	$1,92 \cdot 10^2$	$3,17 \cdot 10^2$
Decyne-3	19,2	17,1	78,3	$1,13 \cdot 10^2$	$2,28 \cdot 10^2$
Naphthenic hydrocarbons					
Cyclobutane	$1,82 \cdot 10^3$	$1,01 \cdot 10^3$	$5,41 \cdot 10^2$	$1,33 \cdot 10^3$	$2,15 \cdot 10^3$
Cyclopentane	$1,94 \cdot 10^3$	$1,37 \cdot 10^3$	$6,37 \cdot 10^2$	$1,47 \cdot 10^3$	$2,44 \cdot 10^3$
Methylcyclopentane	$2,33 \cdot 10^3$	$1,64 \cdot 10^3$	$8,44 \cdot 10^2$	$1,52 \cdot 10^3$	$2,76 \cdot 10^3$
Cyclohexane	$2,76 \cdot 10^3$	$2,14 \cdot 10^3$	$9,36 \cdot 10^2$	$1,74 \cdot 10^3$	$3,17 \cdot 10^3$
Trimethylcyclohexane		$1,05 \cdot 10^3$	$7,48 \cdot 10^2$	$1,38 \cdot 10^3$	$1,66 \cdot 10^3$
1,3-Dimethylcyclohexane	$1,71 \cdot 10^3$				
	$1,25 \cdot 10^3$	$8,09 \cdot 10^2$	$1,01 \cdot 10^2$	$1,12 \cdot 10^3$	$2,16 \cdot 10^3$
Ethylcyclohexane	$1,92 \cdot 10^3$	$1,26 \cdot 10^3$	$6,14 \cdot 10^2$	$1,84 \cdot 10^3$	$2,96 \cdot 10^3$
Trimethylcyclohexane	$1,96 \cdot 10^3$	$1,41 \cdot 10^3$	$6,25 \cdot 10^2$	$2,26 \cdot 10^3$	$3,22 \cdot 10^3$
Propylcyclohexane	$1,33 \cdot 10^3$	70,8	$3,48 \cdot 10^2$	$9,67 \cdot 10^2$	$1,52 \cdot 10^3$
Amylcyclohexane	$1,28 \cdot 10^3$	84,2	$2,36 \cdot 10^2$	$7,34 \cdot 10^2$	$1,18 \cdot 10^3$
Indan	87,1	40,4	$1,09 \cdot 10^2$	$3,48 \cdot 10^2$	$5,85 \cdot 10^2$
Hexahydroindan	$1,82 \cdot 10^3$	$1,51 \cdot 10^3$	64,3	$1,83 \cdot 10^2$	$1,56 \cdot 10^3$
Aromatic hydrocarbons					
Benzene	$5,24 \cdot 10^3$	$1,44 \cdot 10^3$	$7,53 \cdot 10^3$	$1,35 \cdot 10^4$	$2,77 \cdot 10^4$
Toluene	$9,63 \cdot 10^2$	$8,38 \cdot 10^2$	$1,85 \cdot 10^3$	$3,44 \cdot 10^3$	$7,09 \cdot 10^3$
Ethylbenzene	$8,54 \cdot 10^2$	$6,45 \cdot 10^2$	$2,44 \cdot 10^3$	$4,25 \cdot 10^3$	$8,19 \cdot 10^3$
Xylene	$3,92 \cdot 10^2$	$1,28 \cdot 10^2$	$7,74 \cdot 10^2$	$1,47 \cdot 10^3$	$2,76 \cdot 10^3$
Styrene	1,15	0,65	4,45	8,01	14,4

*Translator's note: Cross-reference peak numbers mentioned in Figure caption were omitted in source table.

Table, continued

Substance	Excretion, μg/h				
	exhaled air	sweat	urine	feces	total
n-Propylbenzene	61,3	44,5	$2,39 \cdot 10^2$	$4,08 \cdot 10^2$	$7,53 \cdot 10^2$
1-Methyl-3-ethyl-	81,2	69,2	$2,94 \cdot 10^2$	$7,05 \cdot 10^2$	$1,15 \cdot 10^3$
1-Methyl-4- benzene	$1,03 \cdot 10^3$	83,4	$4,36 \cdot 10^2$	$8,17 \cdot 10^2$	$1,44 \cdot 10^3$
1-Methyl-2- "	92,4	72,6	$3,98 \cdot 10^2$	$7,96 \cdot 10^2$	$1,36 \cdot 10^3$
Butylbenzene	15,4	11,7	35,4	77,8	$1,40 \cdot 10^2$
1,2,4-Trimethylbenzene	12,2	7,45	28,5	62,7	$1,11 \cdot 10^2$
1-Methyl-4-iso-propylbenzene	13,3	11,6	24,3	58,7	$1,08 \cdot 10^3$
1-Methyl-3-iso-propylbenzene	15,4	8,06	29,7	69,3	$1,23 \cdot 10^3$
1,3-Dimethyl-5-ethylbenzene	11,3	9,15	19,8	45,4	85,7
1,2-Dimethyl-4-ethylbenzene	19,1	14,1	30,9	77,2	$1,41 \cdot 10^2$
1,3-Dimethyl-2-ethylbenzene	18,2	17,3	29,4	71,5	$1,36 \cdot 10^2$
1,2,3,4-Tetramethyl-benzene	10,5	8,27	20,5	41,8	81,1
Naphthalene	14,8	10,6	28,4	65,1	$1,19 \cdot 10^3$
2-Methylnaphthalene	5,25	4,38	8,35	18,6	36,6
Oxygen-containing compounds					
I. Aldehydes					
Formaldehyde	30,2	22,4	55,6	$8,57 \cdot 10^3$	$9,65 \cdot 10^3$
Acetaldehyde	$1,21 \cdot 10^3$	$1,47 \cdot 10^3$	$1,86 \cdot 10^2$	$5,92 \cdot 10^3$	$6,37 \cdot 10^3$
2-Methylpropanal	38,3	34,8	64,3	$1,36 \cdot 10^3$	$1,50 \cdot 10^3$
3-Methylbutanal	32,3	26,8	58,4	$9,32 \cdot 10^2$	$1,11 \cdot 10^3$
Pentanal	28,1	25,4	51,9	$8,48 \cdot 10^3$	$9,82 \cdot 10^3$
2,4-Hexadienal	24,1	18,4	46,2	$7,33 \cdot 10^2$	$8,22 \cdot 10^2$
Hexanal	35,4	28,3	61,7	$7,91 \cdot 10^3$	$9,16 \cdot 10^3$
Furfural	25,1	17,2	45,4	$7,16 \cdot 10^3$	$8,04 \cdot 10^3$
Heptanal	29,4	26,6	49,1	$7,44 \cdot 10^3$	$8,49 \cdot 10^3$
Octanal	33,1	31,6	59,4	$7,86 \cdot 10^3$	$9,10 \cdot 10^3$
Benzaldehyde	15,1	10,7	27,2	$4,98 \cdot 10^2$	$5,51 \cdot 10^2$
Nonanal	7,28	6,43	12,2	$2,19 \cdot 10^2$	$2,45 \cdot 10^2$
Decanal	5,37	2,41	7,35	$1,49 \cdot 10^2$	$1,64 \cdot 10^2$
Undecanal	4,23	1,17	8,96	$1,27 \cdot 10^2$	$1,41 \cdot 10^2$
II. Ketones					
Acetone	$3,31 \cdot 10^3$	$2,24 \cdot 10^3$	$3,56 \cdot 10^3$	$1,24 \cdot 10^4$	$1,33 \cdot 10^4$
Methylethyl ketone	$1,12 \cdot 10^4$	$1,97 \cdot 10^4$	$4,54 \cdot 10^4$	$8,97 \cdot 10^4$	$1,66 \cdot 10^5$
2-Butanone	$2,20 \cdot 10^3$	$1,33 \cdot 10^3$	$2,97 \cdot 10^3$	$1,34 \cdot 10^3$	$2,21 \cdot 10^3$
Methylisobutyl ketone	$1,23 \cdot 10^3$	$1,16 \cdot 10^3$	$1,48 \cdot 10^3$	$7,63 \cdot 10^3$	$1,15 \cdot 10^3$
2-Hexanone	$1,36 \cdot 10^3$	$1,02 \cdot 10^3$	$1,74 \cdot 10^3$	$8,07 \cdot 10^3$	$1,22 \cdot 10^3$
4-Heptanone	$1,12 \cdot 10^3$	97,6	$1,36 \cdot 10^3$	$5,41 \cdot 10^3$	$8,87 \cdot 10^3$
3-Octene-2-one	70,1	65,2	$1,04 \cdot 10^3$	$3,13 \cdot 10^3$	$5,52 \cdot 10^3$
2-Decanone	60,8	50,3	97,5	$2,27 \cdot 10^3$	$4,36 \cdot 10^3$
2-Undecanone	50,1	30,4	74,3	$1,85 \cdot 10^3$	$3,40 \cdot 10^3$
3-Methylcyclopentanone	20,7	15,5	58,6	$1,04 \cdot 10^3$	$1,99 \cdot 10^3$
III. Alcohols					
Methanol	$2,68 \cdot 10^3$	$1,21 \cdot 10^3$	$6,64 \cdot 10^3$	$1,63 \cdot 10^3$	$2,68 \cdot 10^3$
Ethanol	$9,68 \cdot 10^3$	$6,35 \cdot 10^3$	$8,15 \cdot 10^3$	$1,02 \cdot 10^4$	$1,26 \cdot 10^4$
Propanol	$9,03 \cdot 10^3$	$7,27 \cdot 10^3$	$2,12 \cdot 10^3$	$9,94 \cdot 10^3$	$1,37 \cdot 10^4$
Isopropanol	$4,12 \cdot 10^3$	$8,35 \cdot 10^3$	$3,47 \cdot 10^3$	$1,36 \cdot 10^4$	$1,90 \cdot 10^4$
Butanol	$6,82 \cdot 10^3$	$6,61 \cdot 10^3$	$9,39 \cdot 10^3$	$7,44 \cdot 10^3$	$9,72 \cdot 10^3$
Cyclohexyl alcohol	$7,04 \cdot 10^3$	$6,86 \cdot 10^3$	$1,14 \cdot 10^3$	$9,61 \cdot 10^3$	$1,21 \cdot 10^4$
Isoamyl alcohol	$6,62 \cdot 10^3$	$5,95 \cdot 10^3$	$9,17 \cdot 10^3$	$8,43 \cdot 10^3$	$1,06 \cdot 10^4$
Benzyl alcohol	$3,08 \cdot 10^3$	$2,41 \cdot 10^3$	$5,26 \cdot 10^3$	$5,32 \cdot 10^3$	$6,40 \cdot 10^3$
3-Methyl-1-butanol	$7,54 \cdot 10^3$	$4,97 \cdot 10^3$	$1,03 \cdot 10^3$	$8,35 \cdot 10^3$	$1,06 \cdot 10^4$
IV. Ethers					
Ethyl acetate	$3,53 \cdot 10^3$	$2,83 \cdot 10^3$	$9,64 \cdot 10^3$	$2,87 \cdot 10^3$	$4,47 \cdot 10^3$
1,4-Dioxane	$7,68 \cdot 10^3$	$5,48 \cdot 10^3$	$1,07 \cdot 10^3$	$5,33 \cdot 10^3$	$7,72 \cdot 10^3$
Butyl acetate	$2,76 \cdot 10^3$	$1,92 \cdot 10^3$	$7,38 \cdot 10^3$	$1,95 \cdot 10^3$	$3,16 \cdot 10^3$

Table, continued

Substance	Excretion, μg/h				
	exhaled air	sweat	urine	feces	total
Isobutyl acetate	$1,62 \cdot 10^2$	$1,37 \cdot 10^2$	$4,47 \cdot 10^2$	$8,64 \cdot 10^2$	$1,61 \cdot 10^3$
Isoamyl acetate	$2,54 \cdot 10^2$	$2,03 \cdot 10^2$	$8,65 \cdot 10^2$	$1,72 \cdot 10^3$	$3,04 \cdot 10^3$
Ethyl hexanoate	$1,23 \cdot 10^2$	94,8	$1,59 \cdot 10^2$	$7,13 \cdot 10^2$	$1,09 \cdot 10^3$
Ethyl octanoate	92,7	65,1	$1,84 \cdot 10^2$	$6,29 \cdot 10^2$	$9,71 \cdot 10^2$
Diphenyl ether	$1,75 \cdot 10^2$	$1,37 \cdot 10^2$	$3,37 \cdot 10^2$	$9,24 \cdot 10^2$	$1,57 \cdot 10^3$
Ethyl butanoate	65,0	59,4	$1,54 \cdot 10^2$	$5,43 \cdot 10^2$	$8,21 \cdot 10^2$
3-Methyl-2-butylacetate	72,4	58,7	$1,97 \cdot 10^2$	$6,59 \cdot 10^2$	$9,87 \cdot 10^2$
V. Other compounds					
Carbon monoxide	$2,71 \cdot 10^4$	$5,03 \cdot 10^3$	$1,62 \cdot 10^3$	$1,53 \cdot 10^5$	$1,87 \cdot 10^5$
Phenol	$3,23 \cdot 10^2$	$5,21 \cdot 10^2$	$4,13 \cdot 10^2$	$2,84 \cdot 10^3$	$7,70 \cdot 10^3$
Furan	$4,27 \cdot 10^2$	$2,31 \cdot 10^2$	$5,48 \cdot 10^2$	$7,36 \cdot 10^3$	$8,57 \cdot 10^3$
p-Cresol	$1,92 \cdot 10^3$	$7,14 \cdot 10^2$	$2,43 \cdot 10^3$	$1,69 \cdot 10^4$	$2,20 \cdot 10^4$
Menthol	$1,81 \cdot 10^3$	92,7	$9,52 \cdot 10^2$	$1,08 \cdot 10^3$	$2,31 \cdot 10^3$
Formic acid	$8,11 \cdot 10^3$	$6,38 \cdot 10^3$	$8,99 \cdot 10^3$	$7,67 \cdot 10^4$	$1,00 \cdot 10^5$
Acetic acid	$1,58 \cdot 10^3$	$1,27 \cdot 10^3$	$1,44 \cdot 10^3$	$9,21 \cdot 10^4$	$9,64 \cdot 10^4$
Nitrogen-containing compounds					
Methylamine	$4,21 \cdot 10^2$	$5,63 \cdot 10^2$	$8,14 \cdot 10^2$	$2,26 \cdot 10^4$	$3,17 \cdot 10^4$
Isopropylamine	$3,49 \cdot 10^2$	$1,48 \cdot 10^2$	$6,83 \cdot 10^2$	$1,76 \cdot 10^4$	$2,49 \cdot 10^4$
Pyrrolidine	0,22	0,66	2,14	6,02	9,07
Indole	0,06	0,09	0,15	2,09	2,39
Skatole	0,06	0,05	0,18	1,27	1,56
2,2-Dipyridyl	13,6	12,7	21,5	81,2	$1,29 \cdot 10^2$
n-Methylpyrrole	18,4	11,4	50,5	97,7	$1,78 \cdot 10^2$
Methylpiperazine	19,4	15,7	61,3	$1,13 \cdot 10^2$	$2,09 \cdot 10^2$
Acetonitrile	$2,36 \cdot 10^2$	$2,03 \cdot 10^2$	$4,48 \cdot 10^2$	$8,29 \cdot 10^2$	$1,72 \cdot 10^3$
Methacrylonitrile	17,4	19,3	52,4	79,3	$1,68 \cdot 10^2$
Sulfur-containing compounds					
Methyl mercaptan	1,62	1,24	12,6	$1,35 \cdot 10^2$	$1,50 \cdot 10^2$
Ethyl mercaptan	2,34	1,56	16,9	$3,06 \cdot 10^2$	$3,27 \cdot 10^2$
Dimethyl disulfide	18,4	17,5	40,3	$1,86 \cdot 10^2$	$2,62 \cdot 10^2$
Amyl mercaptain	2,08	1,05	11,2	15,1	29,4
2,3,4-Trithiopentane	24,5	13,9	44,1	85,7	$1,68 \cdot 10^2$
Allyl thioisocyanate	15,6	10,4	50,1	$1,11 \cdot 10^2$	$1,87 \cdot 10^2$
Ethylene sulfide	28,5	16,6	75,3	$1,28 \cdot 10^2$	$2,48 \cdot 10^2$
Chlorine-containing compounds					
Chloroform	$1,75 \cdot 10^2$	$1,24 \cdot 10^2$	$7,03 \cdot 10^2$	$9,75 \cdot 10^2$	$1,98 \cdot 10^3$
Trichloroethylene	$1,17 \cdot 10^2$	94,5	$5,79 \cdot 10^2$	$6,09 \cdot 10^2$	$1,40 \cdot 10^3$
Tetrachloroethylene	$1,05 \cdot 10^2$	83,8	$2,54 \cdot 10^2$	$5,47 \cdot 10^2$	$9,90 \cdot 10^2$
Chlorobenzene	$1,12 \cdot 10^2$	87,9	$2,13 \cdot 10^2$	$5,93 \cdot 10^2$	$1,01 \cdot 10^3$
Methyl chloride	$1,51 \cdot 10^2$	$1,02 \cdot 10^2$	$2,63 \cdot 10^2$	$8,33 \cdot 10^2$	$1,35 \cdot 10^3$
Carbon tetrachloride	16,8	13,4	85,6	$1,02 \cdot 10^2$	$2,18 \cdot 10^2$
Dichloromethane	$1,32 \cdot 10^2$	$1,18 \cdot 10^2$	$2,18 \cdot 10^2$	$6,03 \cdot 10^2$	$1,07 \cdot 10^3$
1,1,1-Trichloroethane	33,5	28,7	$1,11 \cdot 10^2$	$1,96 \cdot 10^2$	$3,69 \cdot 10^2$

Polymers and other materials or items used in spacecraft will be increasingly refined, as a result of which their role in pollution of the atmosphere of sealed compartments will increasingly decline. However, the intensity of excretion of products of vital functions will remain entirely unchanged, and their role in polluting the air environment will continue to grow. In addition, in order to detect disease or monitor health status, it may be more

efficient to use specific compounds contained in lower concentrations, as compared to the main excreta, which are listed in the table. All this makes it necessary to formulate many concrete tasks, in accordance with which comprehensive special investigations of biological excretions must be expanded significantly.

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CHANGES IN FUNCTIONAL PARAMETERS OF ANIMALS DURING LONG-TERM INHALATION OF ACETIC ACID

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (manuscript received 24 Nov 86) pp 56-60

[Article by V. P. Savina and B. V. Anisimov]

[English abstract from source] Laboratory animals inhaled acetic acid vapors at a concentration of 86 to 27 mg/m^3 for 3 to 35 days. It was found that the dose of 36 mg/m^3 inhaled for as long as 22 days constituted the minimal acting dose. The most sensitive parameters to be used in detecting the toxic effect of acetic acid were: treadmill run duration, open field activity, and ethylene, acetaldehyde and acetone concentrations in the exhaled air.

[Text] Acetic acid (AA) is a regular element in the gas environment of closed systems [8, 14]. However, its toxicology has not been sufficiently studied. There is information concerning the effect of AA fumes in concentrations of up to 5 mg/m^3 with 95-day exposure [11, 12]. The insignificant changes in physiological and biochemical parameters can be attributed to manifestation of adaptation to this factor, rather than a consequence of the deleterious effect of AA. Apparently, in the gas atmosphere of closed systems, a concentration of toxic impurities at which there is manifestation of signs of adaptation to the toxic agents can be considered permissible, but on the condition that the changes that arise are entirely reversible and do not affect work capacity or health [2]. This guideline for regulations can extend only to substances with mild cumulative properties that have no specific effect (allergenic, carcinogenic, etc.). Most anthropogenic toxic substances, i.e., volatile products of human metabolism, including AA and other volatile fatty acids (C_2-C_6), meet this requirement, and the above guideline for setting hygienic standards can be applied to them [3, 4, 13].

We submit here the results of a series of experiments dealing with the effect of AA on animals in the case of long-term inhalation in relatively high concentrations. Our main objective was to obtain baseline data for setting hygienic standards for AA levels in the gas atmosphere of closed environments used for different purposes.*

*The following participated in conducting the experiments: T. I. Golubeva, S. M. Ivanova, I. B. Krasnov, G. N. Kuzmenko, G. P. Tikhonova, V. N. Shvets, V. M. Yakovleva and M. Ye. Yakovleva.

Methods

Animals (rats and mice) were exposed to acetic acid in 200-ℓ chambers. We used a dynamic mode, where air was propelled through the chamber at a volumetric rate of 3.5 m^3/h. Air temperature in the chamber held at 24-27°C and relative humidity constituted 75-85%. Control animals were kept in a similar chamber under identical microclimate conditions. We used Wistar rats in the experiments with base weight of 180-200 g, and male C57Bl, CBA and F_1(CBA×C57Bl) mice weighing 18-20 g.

We conducted a total of 7 long-term experiments using the following concentrations of AA: 86±2 mg/m^3 (3 days), 75±2 mg/m^3 (2 experiments each lasting 17 days and 1 lasting 35 days), 56±5 mg/m^3 (35 days), 36±1 mg/m^3 (22 days), 27±3 mg/m^3 (22 days). In addition, we performed a series of 1- and 2-day experiments with AA in concentrations of 400 to 900 mg/m^3 and 4-5-h exposure to concentrations of 10 to 30 mg/m^3.

The "open field" method as modified in [6] was used to test behavioral reactions.

Threshold summation parameter was determined using the method proposed by S. V. Speranskiy: summation of pulses with progressively increasing voltage (1 pulse/s, pulse duration 200 μs, pulse amplitude was gradually raised by 1 V at a time, from 1 to 20 V). The animals moved freely on the electrodes [1]. Stimulation was recorded according to digital twitching.

After exposure, some animals were put to sleep with ether. Organs were removed and weighed using standard techniques [7]. The animals were decapitated for histological tests. Blood for analysis was drawn from the caudal vein. Formed blood elements were counted by the standard method. Physical work capacity was evaluated only in mice, on the basis of duration of running on a treadmill at tape feeding rate of 12 and 16 ℓ[sic]/min (for different groups of animals). Histological sections were stained with hematoxylin and eosin, and the spleen and thymus with pyronin. Several parameters of erythrocyte metabolism were analyzed. Gas chromatogrpahy was used to determine levels of volatile metabolites in air exhaled by rats: hydrocarbons (C_2-C_5), acetone and acetaldehyde [15]. Samples of exhaled air were collected in polyethylene film containers connected to a mask with valves. The mask was placed on the animal's snout. Samples were collected for 1.5-2 min. At least 10 animals per group were used in all experiments with each method.

Reliability of differences was assessed according to Student or Wilcoxson's criterion, depending on distribution of parameters.

Results and Discussion

After brief exposure to AA in concentrations of 10 to 30 mg/m^3, there was an increase in mouse motor activity, as compared to the control group, apparently due to excitement of animals from the odor of AA. In the long-term experiments, AA fumes led to decrease in activity of rats and all three lines of mice, when present in concentrations of 36 to 86 mg/m^3. Reliable differences were obtained when we compared "overall" activity of animals, including running distance,

frequency of looking into the burrow and number of grooming acts. In a concentration of 27 mg/m^3, AA fumes did not affect the animals' behavior.

Concentrations of 36 to 75 mg/m^3 were found to be active according to measurement of threshold-summation parameter. Inhalation of AA in concentrations of 56 and 75 mg/m^3 elicited reliable ($p \leq 0.01$) decline of capacity to summate pulses, and stimulation threshold increased from 5-7 to 10-14 pulses (means for different groups). In a concentration of 36 mg/m^3, AA led to insignificant decline of stimulation threshold by 1-2 pulses ($p \leq 0.05$).

After exposure to concentrations of 36 mg/m^3 or more, running time decreased for mice by a factor of 1.8-2. Exposure for 24 h to a concentration of 500 mg/m^3 did not affect mouse work capacity.

Experimental rats weighed 15% less ($p \leq 0.01$) than controls as a result of 35-day exposure to AA in a concentration of 75 mg/m^3. There was no difference between parameters of the groups after 17-day exposure to the same concentration. Mice were more sensitive according to this parameter. Thus, by the end of the experiments using AA in concentrations of 56 and 75 mg/m^3, the experimental animals weighed reliably less by 11 and 15%, respectively.

Weight and relative weight (ratio of organ weight in grams to body weight in kilograms) of the spleen dropped significantly after 2-day inhalation of AA in a concentration of 400 mg/m^3 and 1-day exposure to 900 mg/m^3 (by 25-30%). In a concentration of 75 mg/m^3, AA elicited in rats a 10% increase in relative weight of the kidneys and 25% increase in that of the spleen ($p \leq 0.05$) by the 15th day of exposure; this effect persisted to the end of the experiment (35 days).

In CBA and C57Bl mice, AA in concentrations of 56 and 75 mg/m^3 led to significant increase in spleen weight and relative weight. C57Bl mice were found to be more sensitive; this parameter rose in them by 50 and 65%, respectively. Relative weight of C57Bl and CBA mouse kidneys increased by 10% ($p \leq 0.05$) with 75 mg/m^3 AA after 17 days of exposure; by the 35th day of exposure the difference between experiment and control persisted. In F_1 (CBA×C57Bl) hybrid mice, no reliable changes were demonstrated in relative weight of organs.

Histological changes were demonstrated in the rats after exposure to a concentration of 75 mg/m^3 (35 days). Isolated nephrons with impaired microstructure were found in some experimental animals' kidneys. In all experimental rats, the lumen was enlarged in most collecting tubules of the internal zone of the medullary region, the epithelium was flattened, and there were nuclei protruding into the tubular lumen. Toward the end of the experiment there was increase in hemosiderin content of the spleen.

After exposure for 3 days to AA in a concentration of 86 mg/m^3, C57Bl mice failed to reveal any histological disturbances. Exposure to AA in a concentration of 36 mg/m^3 did not lead to any histological changes whatsoever in rats.

No reliable changes in formed blood elements and erythrocyte metabolism were found in any of the experiments.

As we know, excretion of hydrocarbons (C_2-C_5) is a convenient means of in vivo determination of intensity of lipid peroxidation. Intensification of this process is a universal indicator of the effects of extreme factors [15, 16]

Measurement of ethylene, acetone and acetaldehyde in exhaled air can, as shown by our data, serve as a sensitive test for detection of the effect of low concentrations of AA fumes. AA in a concentration of 36 mg/m^3 led to 2-3-fold increase in ethylene level and 2-5-fold increase in acetone on the 1st and 14th days of the experiment. By the end of the exposure period (22d day), acetone concentration dropped to the baseline in experimental animals. With 56 and 75 mg/m^3 AA, there was insignificant decline of ethylene content in exhaled air after 1 day, 2-3-fold increase after 7 days, whereas by the end of the exposure period (22d and 34th days) it virtually returned to the baseline level. Concurrently with increased excretion of ethylene, experimental animals showed 3-5-fold increase in acetone and acetaldehyde content of exhaled air. Acetone and acetaldehyde levels referted to the baseline after 1 week and on the 14th day of exposure. There were no changes in elimination of acetone and acetaldehyde in the control groups.

High concentrations of AA (350±17, 500±23 and 900±25 mg/m^3), with exposure for 1 day, led to significant decline of ethylene level and 8-fold increase in acetone. The change in levels of ethylene and acetone in exhaled air warrants the conclusion that the animals adapted partially to AA fumes. By the end of the 2d week of exposure, elimination of ethylene, acetone and acetaldehyde reverted to normal. The significant decline of ethylene excretion after 1-day inhalation, in the case of both moderate (56 and 75 mg/m^3) and high (350-900 mg/m^3) concentrations, is indicative of change in the process of lipid peroxidation already at the 1st stage of intoxication. It is of considerable interest to identify the mechanism of this phenomenon.

The change in ethylene, acetone and acetaldehyde content of exhaled air is an exogenous manifestation (in the direct and figurative sense) of biochemical processes that develop with AA fume poisoning. Comparison to physiological parameters (open field, threshold-summation parameter, work capacity) shows that a return to normal levels of ethylene in exhaled air does not yet signify that there is no deleterious or depressing effect.

On the basis of the aggregate of changes in the tested parameters, it can be concluded that 36 mg/m^3 is the threshold concentration of AA for mice and rats in the case of continuous inhalation. An AA concentration of 27 mg/m^3 is ineffective. Our results do not agree with the conclusions in [11], where changes were discovered in several biochemical and hematological parameters in the course of 95-day exposure to AA in concentrations of 0.2 and 5 mg/m^3. The threshold dose we obtained is consistent with the results of Sh. Ye. Tokanova, who found that 30 mg/m^3 was the threshold dose of propionic acid in experiments with rats with 30-day inhalation and 100 mg/m^3 with 12-day inhalation [13]. Similar results had also been obtained in earlier studies: 20 mg/m^3 for valeric and caproic acids with 3-week exposure [3, 4], and 15 mg/m^3 for butyric acid with 30-day exposure [9, 10].

Some of the distinctions of action of AA and, perhaps, other volatile fatty acids merit more comprehensive investigation. In particular, we cannot rule

out the possibility of existence of discrete, compensated changes in the kidneys and blood under the effect of concentrations below 27 mg/m^3. Evidently, such changes could be detected by using functional and nonspecific extreme load tests.

According to the conceptions prevailing in Soviet toxicology, the changes in functional parameters found in this series of experiments under the effect of AA fumes are viewed as a manifestation of toxic action. At the same time, within the tested range of concentrations (36-86 mg/m^3), used for many days of exposure, it was not possible to detect a relationship between extent and time of appearance of the biological effect, on the one hand, and concentration of AA fumes, on the other. This could be attributed, it seems to us, to faster adaptation to AA with increase in its concentration in air. Similar effects have been described before [5].

The results of these experiments enable us to undertake investigations on volunteer human subjects and, at the same time, provide us with baseline values in order to set standards for AA fume levels in closed environments.

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PHYSIOLOGICAL AND IMMUNOLOGICAL ASPECTS OF HUMAN ADAPTATION TO TEMPERATURE ELEVATION IN A CLOSED ENVIRONMENT

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[Article by L. N. Mukhamediyeva, I. V. Konstantinova, V. V. Zhuravlev†, Ye. N. Antropova, G. P. Teplinskaya and Ye. I. Nikitin]

[English abstract from source] Physiological and immunological investigations have shown that on day 2 of adaptation to the warming enclosed enviornment the test subjects may develop pustular skin disease. A certain role in the disease is played by the autoinfection process aggravated by sensitization of the organism to autoantigens.

[Text] In the course of forming stable adaptation of the human body to heat factors, along with change in the system of thermoregulation, there is development of nonspecific neurohumoral reactions aimed at enhancing man's resistance to heat. The "emergency" adaptation response, that occurs immediately after exposure to the adverse factor, is also associated with change in immunoresistance [8, 14, 16], the role of which in the pathogenesis of development of skin lesions (miliary erysipelas) [16] is not entirely clear and requires special investigation [7, 11]. Pustular skin lesions are consistently observed during adaptation to inadequate temperatures in closed systems, and they are one of the factors lowering hunan work capacity and limiting the time man can spend under such conditions [3, 7, 11].

We submit here the results of physiological-hygienic and allergological studies, parameters of cell humoral immunity in the course of adaptation to a microclimate where temperature rises under conditions of a closed environment.

Methods

We conducted 3 series of studies with the participation of 25 essentially healthy subjects 20-35 years of age, who were not pre-adapted to high temperatures. Table 1 lists the microclimate conditions in the closed system.

Thermal status of the subjects was determined on the basis of measuring skin temperature at 11 points, rectal temperature (Tr) with determination of weighted

mean skin temperature (WMT) according to Ramzayev (1957). Mean body temperature (MBT) and amount of heat accumulated in the body were calculated using Barton's formula [2]. A resistance thermometer was used to measure skin and rectal temperature.

Table 1. Conditions of investigations

Series	Exposure time, days	Number of subj.	Temp., °C	Relative humidity, %	Barometr. press., mm Hg	Gas composition	
						O_2, %	CO_2, %
I	15	4	20±1,0	90±5	750±10	21±2	0,4—0,6
II	15	4	33±1,0	40±10	750±10	21±2	0,4—0,6
III	15(7)	17	33±1,0	90±5	750±10	21±2	0,4—0,6

Note: Duration of exposure to "temperature-rising" microclimate is indicated in parentheses.

Blood catalase activity was measured by the method of Bakh and Zubkova [12]; serum sodium level by the method of Albenis and Lane, and potassium by the colorimetric micromethod of Lazarov [10]. Acid-base equilibrium of whole blood (ABE) was tested with a micromethod. Venous blood drawn from the cubital vein served as material for the immunological studies. Lymphocytes isolated from peripheral blood were used in a ficoll-pack gradient for identification of T and B cells [17]. T lymphocytes were counted by the method of spontaneous rosette-formation with sheep erythrocytes , E-RFC [21]. Number of B lymphocytes was determined on the basis of their capacity to form rosettes with bovine erythrocytes loaded with M antibodies and the third component of complement, EAC-RFC [17]. The functional state of the overall T lymphocyte population was evaluated by autoradiography, according to rate of incorporation of ^3H uridine by lymphocytes in a 24-h culture, in the presence of phytohemagglutinin [5]. Functional activity of B lymphocytes was evaluated according to amounts of the three main classes of immunoglobulin, A, M and G [19].

Allergological status was evaluated by the method of specific lymphocyte blast transformation (SLBT) in vitro, in the presence of bacterial allergens of the main representatives of human automicroflora: Staphylococcus, Streptococcus, E. coli and Proteus [18]. Specific agglomeration of leukocytes (SAL) in peripheral blood, in the presence of formalin, epichlorohydrin and pyridine [1].

Results and Discussion

In the first series of studies (air temperature 20±1°C, relative humidity 90±5.0%) no changes whatsoever were demonstrable in the parameters in question, with the exception of some decline of basal metabolism, which is inherent in man when in a closed environment; MBT was in the range of 35.0-35.3°C. Kerdo index, as well as retention of temperature topography on the surface of the body, were indicative of absence of stress in autonomic nervous system function. Parameters of ABE were in the normal range, blood pH remained at 7.36-7.43, while carbon dioxide tension was in the range of 34.5-42.5 mm Hg. No changes were demonstrable in the integument.

Table 2. Dynamics of immunological parameters in third series of studies (M±m)

Parameter	Normal fluctuations	Baseline	Stay in closed system, days			Recovery period
			2	5-7	10-13	
Serum Ig content, mg%	G 800-1800 A 100-360 M 80-200	1590±205 257±51 116±12	1980±147 307±56	2163±369** 317±30 117±18	2023±103 422±40** 123±6	1913±142 417±26 118±5
Total T lymphocytes (E-RFC), %	55-85	47.7±2.1	62.0±1.0****	58.0±2.0***	70.0±6.0****	60.6±4.1
B lymphocytes with receptor for activated complement component (EAC-RFC), %	10-30	12.3±2.3	15±2.0	33.3±3.7****	34.3±11.4****	18.4±3.2
Reactivity of total T lymphocyte population (% with high rate of RNA synthesis in 24-h PHA culture)	15-25	20.5±0.8	25±3.8	24.8±5.5	20.7±1.4	19.7±2.0

*Normal fluctuations of parameter were established for men in 25-45-year age group who had undergone a special medical check.

**p<0.05

***p<0.01

****p<0.001

In series II (T_a [air temperature] 33 1°C, relative humidity 30-50%), the subjects rated the microclimate as "warm," and complained of a stuffy feeling at night. We demonstrated 0.3°C elevation of MBT due to elevation of skin WMT. Body temperature showed virtually no change, and heat content increased by a mean of 10.5±0.14 kcal/m^2.

In assessing the immunological status of subjects in the first and second series, we failed to detect appreciable changes.

Under the combined effect of elevated temperature and humidity (third series of studies), the subjects assessed the microclimate in the closed system as hot. Objectively, starting on the 1st day of exposure, we observed 0.6°C elevation of Tr, skin WMT rose by 1.8°C and MBT by 0.9°C. Heat content of the body increased by a mean of 41.5 kcal/m^2/h, apparently due to accumulation of metabolic heat [15] as a result of decline (to 7-8 mm Hg) of physiological shortage of fluid. Maximum heat increment (56 kcal/m^2/h) was observed on the 1st day of the tests. Fluid loss constituted a mean of 2.7 ℓ/day. Smoothing (to 1°C) of oral-caudal and distal-proximal temperature ratios on the skin surface was also indicative of body overheating. Thus, while the skin temperature gradient in the region of the forehead and leg was 3-4°C under optimum microclimate conditions, in the case of a "heating" microclimate the difference diminished to 0.37°C. The proximal-distal temperature difference for the skin of the thigh and leg constituted 0.8°C under optimum microclimate conditions, whereas in a heating microclimate leg temperature exceeded that of the thigh region by 0.44°C. The subjects complained of rapid fatigability, insomnia, heavy headedness and anorexia. On the 2d day and, in some cases toward the end of the 1st day in the closed system, miliary eruption was detected, appearance

of which was preceded by severe itching, in symmetrical segments of the integument in theregion of the hands, dorsal surface of forearms, internal aspects of thighs and, in severe case, over the entire body. By the 2d-3d day, numerous pustules were formed at the sites of eruption, while two subjects also developed conjunctivitis.

On the 1st day of combined exposure to high ambient temperature and humidity, the increase in body heat was combined with a compensated form of metabolic acidosis, which was manifested by drop of carbon dioxide tension to 29-33 mm Hg at oxygen tension of 120-124 mm Hg.

Depression ($p<0.05$) of blood catalase activity and increase ($p<0.01$) in blood sodium content were observed in the subjects by the 7th day of exposure to the heating microclimate.

With respect to immunological status, there was reliable increase in E-rosette forming cells, as compared to the baseline, on the 2d ($p<0.001$), 5th-7th ($p<0.01$) and 10th-13th ($p<0.01$) days in the chamber. An increase in EAC-RFC was observed on the 5th-7th day ($p<0.001$). IgG and IgA levels were reliably higher than baseline values on the 5th-7th and 10th-13th days, respectively ($p<0.05$).

The functional activity of the total population of T lymphocytes, as determined by the PHA [phytohemagglutination] test did not undergo appreciable change throughout the period. In all samples, SAL did not exceed 1.5, which was indicative of absence of sensitization of the subjects to the allergens used--epichlorohydrin, pyridine and formalin. Lymphocyte blast-transformation test with allergens of Staphylococcus, Streptococcus, E. coli and Proteus failed to demonstrate clinically significant sensitization to the main representatives of normal human automicroflora.

Analysis of time of appearance and development of pustular erysipelas as a function of dynamics of immunological parameters revealed that deviations in the immunity system were observed already on the 2d day (elevation of E-RFC), i.e., concurrently with clinical manifestations of skin disease. Maximum changes (elevation of E-RFC, EAC-RFC, IgG) were noted on the 5th-7th day of exposure to high temperature combined with high humidity. Reliable elevation of IgA and E-RFC, as compared to the baseline, persisted on the 10th-13th day. Soon after exiting from the closed system the pathological skin changes disappeared. We also failed to demonstrate reliable deviations of immunoreactivity (Table 2).

Allergological tests performed in our studies did not enable us to obtain direct evidence of sensitization to the allergens used. At the same time, the findings do not rule out the probability of sensitization. It can be assumed that sensitization of the human body did not reach a level that would be demonstrable by the allergological methods used within the time of exposure to the adverse factors (elevated temperature and humidity; 7 days). Elevation of immunoglobulin levels [20] in blood serum, which we observed in the subjects during exposure to a warming microclimate, can serve as indirect confirmation of development of sensitization.

The increase in amount of microorganisms on the mucosa of the human upper respiratory tract and integument, as well as increase in biological activity

of automicroflora in the direction of enhancement of its pathogenic properties, which have been established by a number of authors under analogous conditions, are among the predisposing factors of sensitization [4, 7]. The increase in vascular-tissular permeability, which was observed under overheated conditions and is instrumental in disseminating automicroflora in internal organs, may have had some relevance [11, 14]. It is known, that interaction of microorganisms with toxins and tissues leads to appearance of autoantigens that induce autosensitization [7, 13, 16].

Analysis of our findings and data in the literature warrants the assumption that development of an autoinfectious process aggravated by sensitization to autoantigens plays some part in the genesis of pustular skin lesions, which develop during the period of adaptation to a "warming" microclimate.

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EFFECT OF PYROCETAM ON MOUSE RESISTANCE TO HYPOXIC HYPOXIA 2-3 MONTHS AFTER EXPOSURE TO X-RADIATION

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[Article by A. V. Popov, A. A. Bochenkov, Yu. Yu. Ivnitskiy and Yu. V. Volkovskiy]

[English abstract from source] The resistance of mice to hypoxic hypoxia 3 months after their x-irradiation was evaluated with respect to such parameters as survival rate during the "ascent" to 11,000 m, life time at that altitude and brain succinic dehydrogenase (SDH) and lactate dehydrogenase (LDH) activities at an altitude of 7000 m. Irradiated mice proved to be less resistant to hypoxic hypoxia. SDH activity increased to a greater extent in nonirradiated than in irradiated animals. Pyracetam increased significantly the resistance to hypoxia of both irradiated and nonirradiated mice. SDH activity was stimulated by hypoxia in a greater degree in the pyracetam-treated mice. The resistance to hypoxic hypoxia and SDH activation at an altitude of 7000 m were found to be closely correlated. LDH activity remained essentially unchanged in any of the animal groups.

[Text] Resistance to altitude hypoxia is limited by the adaptation reserve of the central nervous system [2]. The latter, in turn, depends on flexibility of energy-providing mechanisms of the brain [6, 14], which are based on terminal biological oxidation and glycolysis. It is of practical importance to detect states associated with diminished resistance to hypoxia in the absence of visible pathology under normoxic conditions.

It has been established [1, 3] that animals with a history of acute radiation sickness (ARS) develop progressive degenerative changes in brain tissue. Considering the universal pathogenetic role of hypoxia and the high sensitivity to it of nerve tissue, it can be expected that these processes affect energy metabolism of the brain and influence altitude resistance. In spite of the comprehensive study conducted of the latter in the presence of ARS [5], such resistance in patients recuperating at the long postradiation term constitutes an independent problem that has not been sufficiently investigated.

It was previously shown that pyracetam, a nootropic agent, has a beneficial effect on bioenergetic processes in the brain [4].

We undertook this study in order to assess mechanisms of altitude resistance in mice in the ARS recovery period, and explore the possibility of correcting with pyracetam the demonstrated disturbances.

Methods

Male CC57B mice weighing 16-18 g were exposed once to x-rays delivered by an RUM-17 therapeutic unit in a dosage of 4.75 Gy (LD 34/30) at a dose rate of 0.67 Gy/min, anode current of 15 mA, anode voltage of 180 kV, 0.5 m m Cu filter and target distance of 50 cm. Nonirradiated animals served as a control. Two months later the animals were divided into 2 groups: one was given pyracetam for the next 30 days, in the form of suspension, intraperitoneally, in a daily dose of 200 mg/kg; and the other was given saline. Two series of experiments were conducted on the 90th postradiation day.

In the 1st series, we determined mouse tolerance to altitude hypoxia using a method that was modified for these animals [13]. They were exposed in a decompression chamber to 11,000 m altitude (rate of ascent 15 m/s), after which we timed appearance of seizures and apnoe using a stopwatch.

In the 2d series, we tested the effect of moderate hypobaric hypoxia on activity of succinate dehydrogenase (SDH) and lactate dehydrogenase (LDH) in the brain. The experimenters "ascended"with the experimental animals in the chamber to an altitude of 7000 m. The animals were decapitated after 30-min exposure; their brain was excised and placed on ice; then followed the descent and homogenization of tissue. SDH activity in the homogenate was measured by the method in [12]. LDH activity was assessed in the supernatant obtained after centrifuging the homogenate, using a set of reagents. We determined similarly SDH and LDH activity in the brain of animals exposed to normoxic conditions.

We determined the coefficient of correlation for small samples (r) between mean group change in brain SDH activity at 7000 m and mean group time of animal death at 11,000 m.

Results and Discussion

The data listed in Table 1 indicate that 63% of the animals which sustained ARS expired upon reaching an altitude of 11,000 m. In the control, 50% of the mice died. The death rate during ascent to 11,000 m among healthy and irradiated mice given pyracetam constituted 25 and 20%, respectively. Thus, we demonstrated differences in mortality during ascent to 11,000 m. It was higher in irradiated animals than the controls. Pyracetam increased survival significantly in both groups of mice.

Control animals remained viable for a longer time at 11,000 m that irradiated ones. For control mice given saline, death occurred on the average after 19.91±0.96-min exposure to 11,000 m, whereas in those given pyracetam death occurred within 31.00±3.80 min. These parameters constituted 2.50±0.80 and

7.00±2.20 min, respectively, in irradiated mice. Thus, pyracetam improved tolerance to altitude hypoxia in both groups.

Table 1. Mouse resistance to hypobaric hypoxia

Animal group (treatment)	Tolerated ascent to 11,000 m, %	Parameters of hypoxia resistance at 11,000 m, ($\bar{X}\pm m$) min	
		onset of seizures	onset of apnea
Control (n = 28)	50	13,75±3,50	19,91±0,96
Pyracetam (n = 28)	75	24,50±7,40	31,00±3,80*
Radiation (n = 30)	37	1,60±0,40**	2,50±0,80***
Radiation + pyracetam (n = 30)	80	5,40±1,30****	7,00±2,20

*$P_{1-2}<0.05$
**$P_{1-3}<0.01$
***$P_{1-3}<0.001$ [sic]
****$P_{3-4}<0.05$

Table 2. Effect of hypobaric hypoxia on SDH and LDH activity in mouse brain tissue

Animal group (treatment)	SDH activity, nmol triphenyl tetrazolium chloride/g wet tissue/min		LDH activity, μmol/g/wet tissue/min	
	normal conditions	7000 m	normal conditions	7000 m
Control	24,60±1,40 ($n = 11$)	33,23±1,10* ($n = 11$)	36,85±0,11 ($n = 11$)	36,57±0.20 ($n = 11$)
Pyracetam	21,07±0,83 ($n = 12$)	34,73±0,10* ($n = 11$)	31,90±0,11 ($n = 12$)	32,08±0,25 ($n = 11$)
Radiation	26,63±0,83 ($n = 11$)	33,23±0,57* ($n = 12$)	34,10±0,12 ($n = 11$)	34,96±0,21 ($n = 12$)
Radiation + pyracetam	27,00±0,60 ($n = 9$)	35,87±0,83* ($n = 9$)	30,15±0,12 ($n = 9$)	30,19±0,20 ($n = 9$)

*$P<0.001$

Table 2 lists data on SDH and LDH activity in the mouse brain under normoxic conditions and at 7000 m. After 30-min at 7000 m, we observed an increase in SDH activity in all groups, without reliable changes in LDH activity. SDH activity increased more significantly (by 64.8 and 32.9% in healthy and irradiated animals, respectively) in the brain of mice given pyracetam.

Thus, less adaptability of brain SDH was demonstrated in mice which had sustained ARS, with regard to hypobaric hypoxia than in intact animals. A positive correlation ($r = 0.96$) was found between mean group SDH activation at 7000 m and mean group time of death at 11,000 m. LDH activity in the brain does not depend on hypoxia, and it shows little change at the tested times under the effect of both radiation and pyracetam.

As we know, SDH is among the so-called "adaptive enzymes," the activity of which changes appreciably under the influence of various regulatory factors, whereas LDH is a constitutive enzyme, and its activity is relatively constant [9]. Elevation of SDH activity in the brain has been described in the presence of normobaric hypoxia [6]. In the presence of hypoxia due to intensive physical exercise, SDH activity of lymphocytes increases in conditioned people, whereas in unconditioned ones, who have a higher baseline level of activity of this enzyme, it decreases [10]. The hypothesis has been expounded that the capacity to mobilize reserve SHD activity is an indicator of adaptation to various types of acute hypoxia [8, 10]. Evidently, the physiological role of increase in SDH activity under hypoxic conditions is attributable to the fact that, under such conditions, succinate is the only substrate capable of transmitting electrons to the respiratory chain [6, 8].

The obtained data are indicative of decline in mouse resistance to altitude hypoxia in the period of residual effects of acute radiation sickness, and partial normalization of this parameter under the effect of pyracetam. Since a decline in altitude resistance of animals is not inherent in ARS [5], while radiation-induced encephalopathy in recovering patients is demonstrable only at times comparable with those studied here [1, 3], it can be assumed that the decline of resistance to hypoxia is related to pathological changes in nerve tissue that develop at this time. Impairment of compensatory activation of SDH in the brain in response to hypoxia is probably one of the elements in the mechanism of this phenomenon.

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DIAGNOSTIC VALUE OF SOME LOAD TESTS IN EVALUATION OF NONSPECIFIC ELECTROCARDIOGRAPHIC CHANGES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (manuscript received 26 Jul 86) pp 67-69

[Article by V. M. Kondrakov, V. I. Koledenok, P. M. Suvorov and L. I. Arsenyeva]

[English abstract from source] The paper describes the examinations of 353 patients with various cardiovascular pathologies and changes in the end-portion of the ECG ventricular complex. For that purpose potassium chloride, obsidan, orthostatic and hyperventilation tests were used. The examinations demonstrated that the ECG changes were of functional nature in 178 patients, of organic nature in 155 patients and of mixed nature in 20 patients which was important for reliable diagnostic and expertise conclusions.

[Text] Evaluation of changes in the end section of the ventricular complex on the electrocardiogram (ECG) in the form of decline of S-T segment, flattening, biphasic pattern or inversion of T wave presents some difficulties, since these changes are often nonspecific. Such disturbances are encountered not only in the presence of ischemic heart disease (IHD), but functional diseases of circulatory organs. For this reason, the diagnosis of IHD is often made without sufficient grounds, while functional diseases are evaluated as organic heart pathology. In such cases, diagnostic mistakes constituted up to 30-60% [2, 3, 6, 12], and this is due to improper interpretation of general clinical findings, overestimation of results of laboratory and instrument tests.

Our objective here was to make a clinical diagnostic evaluation of the role of a set of functional tests in differential diagnostication of coronarogenic and noncoronarogenic changes in the myocardium, as applied for purposes of expert medical evaluation of flight personnel.

Methods

We tested 353 people 19-52 years of age, in whom the resting ECG revealed changes in shape and/or polarity of T waves. These individuals were divided into two groups on the basis of results of general clinical examination. The first group consisted of 189 people (average age 31.3±2.4 years). Clinically, there was prevalence of symptoms inherent in vegetovascular dystonia: emotional

instability, lability of arterial pressure (BP) and pulse rate (PR), persistent red dermatographism, hyperhidrosis, etc. The second group consisted of 164 people (mean age 46.1 3.2 years). These individuals experienced periodic apnea and intermittent pulse during exercise. Most of them had different combinations of 2-3 risk factors for IHD (smoking, obesity, hyperlipidemia and high BP). None of the subjects had a history of myocardial infarction and none complained of chest pain. According to the results of the general clinical examination, these patients presented with hypertrophy of the left ventricle, attenuation of first sound at the apex of the heart, accentuated second sound over the aorta, flattening of the aortial arch and metabolic changes typical of coronary atherosclerosis (hypercholesterolemia in 58.7%, hyper-β-lipedemia in 55.4%). Polycardiographic data revealed that most subjects had the phasic syndrome of hypodynamia--functional deficiency of the myocardium.

Functional studies (other than routine ECG) included tests with potassium chloride and obsidan [inderal]. In addition, the orthostatic test and test with voluntary hyperventilation were performed on some of the subjects.

Obsidan, in a dosage of 0.5 mg/kg weight, and potassium chloride, in a dosage of 1.0 g/10 kg, were given on different days. ECG was recorded in the 12 conventional leads in the baseline state, as well as 1 and 1.5 h after intake of the last portion of medication.

The active orthostatic test was performed for 30 min. At this time, the subjects stood erect without moving. The ECG was recorded in the 12 conventional leads in recumbant position and after change to erect position, then every 15 min while standing, immediately after the test and in the first 5 min of the recovery period (recumbent position).

The test with voluntary hyperventilation consisted of taking rapid (30-50/min) breaths of maximum depth for 1 min, recording the ECG in the 12 standard leads before the test and immediately after it, as well as every 30 s for the first 3 min of rest.

Results and Discussion

There was complete normalization of the ECG in 158 subjects of the 1st group and only insignificant increase in voltage of T wave in 31 subjects under the effect of potassium chloride. The ECG did not change in 120 subjects of the 2d group, 28 showed deeper inversion of T waves and only 16 showed partial improvement of the end segment of the ECG ventricular complex in some leads. Thus, the result of the potassium test was distinctly positive in 83.6% of the 1st group, and negative in 90.2% of the 2d. The partial decrease in repolarization changes in some ECG leads of 16.4% of the subjects in the 1st group and 9.8% in the 2d was not of differential diagnostic value.

The obsidan test was performed with 167 people of the 1st group and 139 of the 2d. In 148 patients of the 1st group, repolarization disturbances of the myocardium disappeared entirely under the effect of obsidan, and there was insignificant improvement of the ECG in 19 cases. The ECG showed no change in 68% of the 2d group, intensification of repolarization changes in 41 cases, and insignificant increase in T-wave voltage in 2-3 leads in 30 cases. Consequently, the results of the test with obsidan were evaluated as positive in 88.6% of the

1st group, and as negative in 78.4% of the 2d group. The insignificant improvement of the ECG in 11.4% of the patients in the 1st group and 21.6% of the 2d was of no differential diagnostic value.

According to the literature, hypersympathicotonic mechanisms, or disturbances in electrolyte transport through cell membranes are the basis of the repolarization disturbances in the myocardium in the presence of functional cardiovascular disease. Intake of potassium in such cases normalizes membrane gradients of electrolytes, which determine processes of depolarization and repolarization, whereas obsidan (inderal) has a blocking effect on adrenergic structures of the heart, leading to normalization of the ECG [1, 4, 8, 13, 14]. This could explain the demonstrated changes in the end segment of the ECG ventricular complex in most of the 1st group of patients.

In the presence of organic myocardial disease, hypersympathicotonic influences may be insignificant or virtually lacking, while the disturbances in electrolyte transport through cell membranes are not eliminated when the concentration of potassium in extracellular fluid is increased. Consequently, the negative results of drug tests with potassium and adrenoblocking agents in most patients in the 2d group is very probably indicative of organic changes in the ECG [1, 3-6].

It was more difficult to interpret the results of tests on patients in whom one or both drug tests led to insignificantly positve ECG dynamics. For this reason, in order to further pinpoint the causes of repolarization disturbances of the myocardium, we additionally ran the orthostatic and hyperventilation tests on 50 subjects in the 1st group and 46 in the 2d. We demonstrated an effect from the orthostatic test in the form of sagging S-T segment, significant decrease, dual phases or inversion of T waves in most leads in 39 patients of the 1st group and 9 of the 2d. The differences in changes in shape and amplitude of waves and ECG intervals were probably related to the state of regulatory mechanisms of compensating the hydrostatic effect. Since there was redistribution of blood flow, change in position of the heart and increase in function of the adrenosympathetic system during the orthostatic test, a hyperreaction developed in individuals with impaired regulation of the circulatory system, which was associated with significant discharge of catecholamines that caused even more marked ECG changes [6, 10, 17]. Under such conditions, there were insignificant hypersympathicotonic influences on the cardiovascular system of most subjects in the 2d group, and for this reason they did not lead to worsening of processes of repolarization in the myocardium, as confirmed by the less marked increase in heart rate and rise of BP at the height of the test in the 2d group, as compared to the 1st (HR 128.3±3.4/min, BP 148 6±3.3 mm Hg in the 1st group, versus 88.2±4.6 and 136.2±2.9 in the 2d; $p<0.01$).

This test seldom leads to serious ECG changes in the presence of atherosclerotic cardiosclerosis. This disease is characterized by a stable ECG in both recumbent and erect position [6, 8, 11].

ECG changes identical to those observed in the orthostatic test were demonstrated in 33 out of 50 subjects in the 1st group after hyperventilation, whereas the ECG remain stable after forced breathing in 17 subjects of the 1st group and 46 of the 2d.

It is assumed that hypocapnia and respiratory alkalosis develop with hyperventilation, as well as decrease in intracellular potassium concentration and increase in endogenous catecholamine discharge. As a result, the terminal segment of the ECG ventricular complex may change, simulating signs of coronary insufficiency [8, 10, 11]. Such an effect is usually quite distinct in the hyperventilation test on patients with autonomic instability and psychoemotional disturbances. However, no appreciable changes are demonstrable on the ECG of most patients with IHD during hyperventilation [7, 9, 10].

Thus, the results of functional tests on 178 (94.2%) of the patients in the 1st group enabled us to confirm the functional genesis of demonstrated ECG changes. In contrast, the negative results of these tests in 155 (94.5%) of the patients in the 2d group were indicative of organic changes in the end portion of the ECG ventricular complex, i.e., the diagnosis of IHD is most probable for them. Apparently, the ECG changes in 11 (5.8%) of the patients in the 1st group and 9 (5.5%) of the 2d are attributable to a mixed mechanism, since they occurred in different directions with the functional tests.

Consequently, the set of functional tests we used enables us to define the genesis of changes in the end segment of the ventricular complex on the ECG and verify the diagnosis, which is extremely important in examining and making expert evaluation of flight personnel.

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USE OF BIFIDUMBACTERIN FOR CORRECTION OF INTESTINAL DYSBACTERIOSIS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (manuscript received 2 Feb 86) pp 70-72

[Article by N. N. Lizko and G. I. Goncharova]

[Text] The prospect of long-term manned spaceflights advances a number of new problems for space biology and medicine, among which ecology of microorganisms and interaction of the macroorganism with its autoflora acquire importance.

Adverse environmental factors and stress lead to disruption of normal ecological relations, in particular, with regard to composition of intestinal microflora. The dysbiotic nature of changes is associated with dramatic decline in level of bifidobacteria and lactobacilli, impairment of quantitative ratio between bifidobacteria and E. coli [4]. It was established that there is an increase in quantity of conditionally pathogenic microorganisms, E. coli with altered enzymatic activity and diminished antagonistic properties, clostridia, bacteria of the genera Klebsiella, Proteus, Pseudomonas and others, immediately after the decrease in bifidobacteria and lactobacilli until they are entirely reduced. In turn, the increase in conditionally pathogenic microorganisms, in the presence of shortage of bifidoflora, may be the cause of both intestinal dysfunctions and intestinal infections.

Man's prolonged isolation with concurrent exposure to a number of spaceflight factors could lead not only to changes in composition of autoflora, but attenuation of the body's defenses and increased susceptibility to pathogens of infections, including representatives of automicroflora [3, 4]. It was also established that dysbacteriosis has an adverse effect on intestinal secretory function, processes of absorption and some parameters of protein, lipid and mineral metabolism [2]. Stability of autoflora and its balance have a specific effect on human health and well-being.

Since the importance of the role of bifidoflora in maintaining a normal microbiocenosis in the intestine is unquestionable, while its prevalence not only prevents manifestation of pathogenic action of a number of microorganisms, but enhances resistance to infections, we decided to institute steps to correct the composition of intestinal microflora in individuals exposed to extreme conditions. Intake of bifidumbacterin was prescribed for one of our subjects

who spent 7 days in a hyperbaric chamber with altered microclimate and gas composition of the atmosphere (temperature 35°C, humidity 90% and CO_2 content 3.7%) Incidentally, bifidobacteria were not detected in him at the first examination, and lactobacilli were down to $6 \cdot 10^4$/g feces. E. coli prevailed in the microbiocenosis and was isolated in amounts of $4 \cdot 10^8$. In the second bacteriological test, immediately after our experiments, the bifidoflora of the subject given the above-mentioned agent began to prevail in the microbiocenosis and its quantitative level per gram feces constituted $2 \cdot 10^8$; lactobacilli increased to $2 \cdot 10^6$, and E. coli decreased to $2 \cdot 10^6$. Thus, intake of bifidumbacterin was effective and normalized the intestinal microflora.

The second subject, who was exposed to the same microclimate, did not take the antibiotic. Upon examination of intestinal microbiocenosis before the experiment we failed to demonstrate appreciable deviations from normal. Upon termination of the experiment, this subject showed a decline, by a factor of 10 (from $5 \cdot 10^7$ to $3.8 \cdot 10^6$ and $6.0 \cdot 10^5$ to $8 \cdot 10^4$, respectively) in bifidoflora and lactoflora, and a dramatic increase in conditionally pathogenic enterobacteria of the genera Citrobacter, Klebsiella and Enterobacter (from 0 to $2 \cdot 10^6$).

Thereafter, bifidumbacterin was also prescribed for one of two subjects who spent 14 days in the hypobaric chamber and were given Chlorella protein in their diet. The second subject did not take this agent. Before the experiments, no changes had been demonstrable in either subject with respect to intestinal microbiocenosis. Bacteriological examination on the 15th experimental day revealed dysbacteriosis in the subject who did not take this agent (see Table). He showed a dramatic decrease in bifidobacteria and lactobacilli, and there was prevalence of E. coli in the microbiocenosis. Use of bifidumbacterin for the first subject was effective. We failed to detect disturbances in intestinal microflora after 2-week intake of Chlorella protein as part of his diet.

Normalizing effect of bifidumbacterin on intestinal microbiocenosis

Subjects	Microflora	Before tests	After tests
One given bifidumbacterin	Bifidobacteria	$5 \cdot 10^8$	$1 \cdot 10^9$
	Lactobacilli	$6 \cdot 10^7$	$4 \cdot 10^5$
	E. coli	$2 \cdot 10^8$	$1 \cdot 10^6$
One not given bifidobacterin	Bifidobacteria	$5 \cdot 10^8$	$4 \cdot 10^6$
	Lactobacilli	$5 \cdot 10^7$	$2 \cdot 10^4$
	E. coli	$8 \cdot 10^6$	$6 \cdot 10^7$

Bifidumbacterin was also recommended for a group of people (3) in the recovery period following 182-day antiorthostatic [head-down tilt] hypokinesia, since their intestinal microbiocenosis was indicative of changes in microecology, and it was characterized by changes in anaerobic and aerobic microflora, with increase in number of conditionally pathogenic microorganisms, among which there was prevalence of clostridia and bacteria of the genus Citrobacter. After using this agent, the composition of intestinal microflora showed normalization in the recovery period in all subjects who took bifidumbacterin:

no clostridia were demonstrable, proteus was isolated at the rate of 2.2±0.4 log/g, conditionally pathogenic enterobacteria of the genus Citrobacter at the rate of 4.3±0.6 log/g, whereas in subjects who did not take this agent (3 people) clostridia were present at the rate of 5.4±1.7 log/g, proteus 3.2±0.4 log/g and conditionally pathogenic enterobacteria 5.4±0.9 log/g.

The results of microbiological studies, which were obtained with ground-based simulation of spaceflight conditions, were corroborated during spaceflights. Our studies indicate that certain changes were observed in composition of intestinal microflora of cosmonauts involved in short-term missions. Bifidoflora and lactoflora were the most labile. We must stress the fact that we discovered changes in the microbial cenosis of the intestine in most cosmonauts already in the prelaunch period, as the result of nervous and emotional stress.

Our objective was to restore the bifidoflora in the preflight period with use of bifidumbacterin. The wide use in health care practice of this agent, which is a eubiotic that has a beneficial effect on normalizing the microbiocenosis in both children and adults [1], as well as the beneficial effect obtained with intake of bifidumbacterin by individuals in a closed environment with altered living conditions, with inclusion of biomass of unicellular algae in the diet and intake of the agent in the recovery period following 182-day hypokinesia, served as grounds for our use of bifidumbacterin. The beneficial effect obtained in the cited case enabled us to use the agent for correction of dysbacteriosis of the intestine in cosmonauts during their work. There were eight people under observation.

In this group, bifidobacterium content constituted 7.9±0.5 log/g, while conditionally pathogenic enterobacteria and clostridia were present in high number (6.2±0.8 and 6.6±0.8 log/g, respectively) before the agent was used. After intake of bifidumbacterin, there was significant increase in bifidoflora content (8.7±0.2 log/g), while the number of conditionally pathogenic enterobacteria and clostridia decreased dramatically (4.8±0.7 and 2.9±1.1 log/g, respectively), reachings values inherent in the norm for all of the above-mentioned groups of microorganisms.

On the ground, one can use a commercial product put out in our country by a number of enterprises under the Ministry of Health. However, the benefit from using bifidumbacterin to correct dysbacteriosis in cosmonauts, not only in the preflight period, but during spaceflights, confronted us with the task of finding a form of this agent that would be convenient to transport and use under these conditions.

Intake of bifidumbacterin in tablet form by crew members of both short- and long-term space missions yielded good results.

Development of a lactate product using a strain of bifidobacteria that sours milk was another aspect of our investigations. The lactic bifidumbacterin that was developed has good organoleptic properties and contains 10^8-10^9 viable bifidobacterium cells/mℓ product. Testing of this product on healthy adults revealed that its flavor was good and that it normalized intestinal function.

In the period of professional training of 7 cosmonauts, in whom a low level of bifidoflora (7.6±0.7 log/g) was found, they were given lactic bifidumbacterin for 10 days, at the rate of 100-150 mℓ once a day. Normalization of bifidoflora content was demonstrated (8.9±0.5 log/g; $p<0.001$).

Lactic bifidumbacterin can be recommended for cosmonauts in the preflight period and during recovery following spaceflights. It may also find application for other groups requiring normalization of intestinal microbiocenosis.

There may be different means of stabilizing and restoring the bifidoflora. We have shown that it is possible, in principle, to enrich dehydrated fruit juices (apple, apricot, black currant, cherry), lyophilized cheeses and other foods with bifidobacteria. Data have been obtained indicating that there is good survival of bifidobacteria when such foods are stored for 3-5 years (duration of observation time), and that there are no changes in their flavor when bifidobacteria are added to them.

Thus, the forms of the product that we developed--dry bifidumbacterin, bifidumbacterin in tablet form based on B. bifidum strain I and lactate product using a specially selected strain of bifidobacteria, B. longum B 379M as the ferment, as well as lyophilized foods enriched with bifidobacteria--can find wide application in both biomedical support of spaceflights and health care practice.

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BRIEF REPORTS

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REGULATION OF ENERGY METABOLISM DURING PARACHUTE JUMPS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (manuscript received 5 Feb 87) pp 72-73

[Article by M. M. Dyakonov and V. R. Persianova]

[Text] Virtually all people who make parachute jumps, regardless of how long they trained for them and number of jumps, display considerable nervous and emotional tension. It was previously shown that the nervous and psychological tension before jumps increases utilization of energy [5]. Thus, when parachutists are on the ground, calm and in seated position, they expend 96 kcal/70 kg weight/h. Upon receiving the announcement that jumps are to begin, energy expenditure increases to 112-117 kcal/70 kg/h, reaching 248 and even 270 kcal/h at the time of the jump [5, 7]. Later on, it was established that these changes in expenditure of energy are related to elevation of level of energy metabolism at relative rest, by 11% in comparison to the baseline, with concurrent 15% increase in pulmonary ventilation ($p<0.01$ for both parameters) and increase in respiratory quotient [4].

The foregoing served as grounds for deeper investigation of bioenergetic processes that take place at the time of making parachute jumps.

Methods

In addition to testing gas exchange during the jump [3], we conducted tests by the method of I. S. Balakhovskiy [1, 2] which enabled us to assay the levels of sugar, ATP, cholesterol (Ch) and other components in microquantities of capillary blood.

All of the subjects (19-21 years old) had at least 1 year of experience in parachute jumping and each had made 10-20 jumps. Blood was drawn immediately after landing. The data obtained in the baseline period reflect the level of the tested metabolites at 0700 hours, i.e., after a calm night's sleep and before breakfast. The subjects had nothing to eat for 12 h after the jump.

Results and Discussion

Energy expenditure at the time of the jump ranged from 242 to 285 kcal/h, with a high respiratory quotient (1.0-1.1) ($n = 6$). It should be noted that all of

the subjects carried an additional 26-28 kg (over and above the regular weight carried for parachute jumps).

Dynamics of main energy metabolites of blood during parachute jumps

Subject	Glucose			ATP, mg%		Total Ch, mg%		
	base-line	moment of landing	12 h after land.	base-line	moment of land.	base-line	moment of land.	12 h after
1	103	117	93	43,7	47,3	150	159	213
2	102	120	80	48,2	44,2	147	147	159
3	98	96	75	47,3	37,3	140	163	169
4	103	107	80	59,5	41,9	139	133	143
5	93	99	87	36,9	34,2	99	112	135
6	92	97	86	40,6	27,3	125	80	117
7	102	107	93	45,1	43,9	126	133	136
8	143	100	85	47,3	40,0	104	111	114
9	114	96	85	35,7	34,6	173	175	180
10	100	85	95	39,3	37,5	136	143	165
$\bar{X}_{10}$	105	102	86	44,4	36,9	134	136	155
P			$<0,05$		$<0,05$			$<0,01$

As can be seen in the table, all blood metabolites determining energy metabolism "responded" reliable in a significant number of cases to the jumps and subsequent 12-h activity without intake of food. For example, while blood sugar level virtually failed to change on the average for the group at the moment of landing, as compared to the baseline, it was reliably lower 12 h later. The dynamics of this parameter warrants the assumption that carbohydrate supply was inadequate in some subjects 12 h after the jumps, which could be due to the long interval between meals. At the moment of the jump (see Table), there is significant activation of energy metabolism, some part of ATP, which is a universal energy source, is expended. ATP level dropped reliably in most subjects and on the average for the group ($P<0.05$).

The nature of fluctuation of blood sugar and ATP leads us to conclude that, at the moment of making parachute jumps, there are changes in glycolytic processes, in particular, there is inhibition of ATP synthesis. We believe that this biomechanism may explain the high energy expenditure demonstrated at the time of the jump.

The dynamics of total blood Ch, considering existing information concerning the rate of incorporation of lipid components in metabolism [6], is indicative primarily of the fact that the actual parachute jump is a stress factor for some of the subjects. It should also be noted that the extent of utilization of the lipid component in implementing energetic processes in the body apparently increased, especially in the 12-h period following the jump.

Our findings enable us to make a deeper evaluation of changes in energy metabolism that occur during parachute jumps and subsequent activity; they enable use to advance suggestions for correction of the diet under such conditions. It is deemed desirable to have a rather high amount of readily assimilated carbohydrates in the diet on days when jumps are to be made and the preceding

days. This suggestion is consistent with the recommendations offered by I. G. Popov for preflight diets [8, 9]. At the same time, it is not desirable to postpone meals for too long in the period following jumps.

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UDC: 612.014.482.5-08

SIMULATION OF EFFECT ON BIOLOGICAL SYSTEMS OF IMPACT WAVE FROM HEAVY CHARGED PARTICLE TRACK

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (manuscript received 16 Jun 86) pp 73-76

[Article by Ye. Ye. Kovalev, O. D. Brill, L. V. Nevzgodina, L. I. Ivanov and V. A. Yanushkevich]

[Text] There are specific distinctions to the effect of heavy charged particles of galactic cosmic rays on biological systems during spaceflights, and the mechanism of this effect has not yet been explained in a number of instances. Thus, in experiments dealing with the effects of heavy charged particles on biological systems, which were conducted in space and on accelerators, it was found in a number of cases that there was a deleterious effect at a distance from the ionization track of a particle that exceeded significantly the maximum range of δ-electrons in the environment. For example, when exposing the brain of rats and other laboratory animals to fast heavy ions, the area of damage was substantially larger than the size of the ionization track [7]. In experiments with Bacillus subtilis cells, cell damage was observed at distances of 1-4 μm or more from the track of a heavy ion, whereas the ranges of δ-electrons could not exceed 1 μm [6]. Finally, there are many experiments indicating that the biological effect of heavy charged particles is much greater in a number of cases than is found according to dose calculations, in which only ionization loss in the environment is taken into consideration. Some authors relate such effects to possible nonionizing and relatively remote-acting radiation, type of thermal radiation and impact wave arising in the track of a heavy charged particle [6, 4]. A number of authors have mentioned the possibility of formation of an impact wave with excessive heating and change in aggregate state of a substances in the track of a heavy charged particle [1, 3].

Generation of an impact wave in the core of a heavy charged particle track at the end of its range, in water, was discussed in [4], where ionization loss was so great that the volume density of energy release in the track core exceeds the critical level, and there is formation of a rapidly expanding plasma space, from which the impact wave is emitted, and its energy may constitute a significant share of the energy absorbed in the track core. According to estimates made in the above study, the amplitude of impact wave pressure in water may reach 10-20 atm at a distance of tens of micrometers from the track boundary. There is no information in the literature concerning the effectiveness of impact waves on biological microsystems, and for this reason we cannot

assess the biological effect of an impact wave generated in the track of a heavy charged particle. Our objective here was to test the effect of impact waves simulating impact waves from the track of a heavy charged particle on Lactuca sativa lettuce seeds. To simulate such impact waves, those generated with absorption of intensive laser pulses of short duration are the most suitable. The mechanism of formation of impact waves with absorption of high-power nanosecond- and picosecond-pulses of laser radiation has much in common with the mechanism of formation of an impact wave in a heavy charged particle track: energy is transmitted in a very short time, and one can obtain a volume density of heat release corresponding to any actual ionization density in the track.

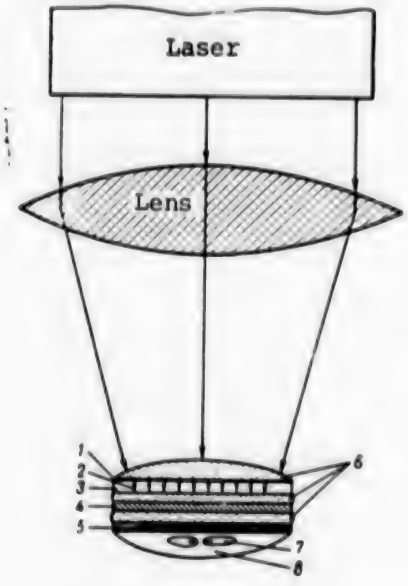

Figure 1.
Diagram of exposure of biological systems to radiation
1) enamel
2) flat impact wave
3) plexiglas
4) copper
5) aluminum
6) PVA
7) seeds
8) epoxy resin

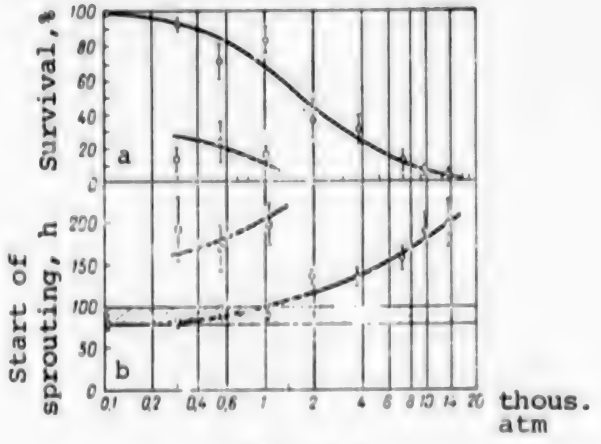

Figure 2.
Survival rate on 10th day (a) and delay in sprouting (b) of dry seeds (○) and swollen seeds (□) of lettuce exposed to impact wave as a function of pressure amplitude in impact wave-front

Methods

In this experiment, we used a flat impact wave generated upon absorption of a 50-ns laser pulse, with energy of 10-15 J, in a thin opaque layer of black enamel about 1 cm^2 in area, in order to obtain stable and controlled conditions of delivering radiation to the biological systems. A GOS [State Standard] 1001 neodymium glass laser operating in the mode of modulated Q factor served as the source of radiation. The diagram showing how the biological systems were irradiated is illustrated in Figure 1. The amplitude of impact wave pressure at the output from the absorbing layer, which was estimated, constituted about 10,000 atm. We placed several discs 0.2-0.5 mm in thickness made of substances with dramatically differing acoustic impedances, matched in such a way as to obtain the required pressure in the preceding wave on the interface of layers as a result of back reflection of the impact wave, on the route of the impact wave in order to lower amplitude to thousands and hundreds of atmospheres.

Air-dried Lactuca sativa lettuce seeds, with relative moisture content of 6%, and swollen seeds were exposed to radiation. The seeds were 3-4 mm in length and 0.5-1 mm in diameter. Before irradiation, the seeds or seedlings were secured, 10 at a time, using polyvinyl alcohol (PVA) along the radii of the bottom disc in such a way as to have the seed ends touching in the center of the disc. With such arrangement of the seeds, the central part of the flat impact wave, which underwent minimal distortion when passing through the stack of discs, reached the most sensitive zone of the seeds and seedlings, the root apical meristem, on the condition of which depend growth and further development of plants.

Immediately after irradiation, the biological specimens were immersed in distilled water for 10 min to remove PVA and transferred to moistened filter paper in Petri dishes for germination. Some of the germinated seeds were fixed in a mixture of acet-alcohol (1:3 ratio), then we performed cytogenetic analysis of the rootlets in the first mitosis on temporary preparations stained with orsein. The effect was assessed according to intensity of sprouting, shift of start of seed germination, number of surviving seedlings on the 10th post-radiation day, as well as yield of aberrant cells and number of dividing cells in seedlings of irradiated seeds, as compared to controls. In all, there were 3 series of irradiation within 4 months. In each series, the biological objects were irradiated at several amplitudes of impact wave pressure in the range of several hudnred to 13,000 atm. Seeds taken from the same batch as those exposed to radiation served as a control.

Results and Discussion

The results of the biological studies with the seeds are submitted in the form of survival of dry and swollen seeds on the 10th postradiation day (Figure 2a) and delay in start of germination (Figure 2b) and intensity of cell division per seed (Figure 3) as a function of impact wave pressure amplitude.

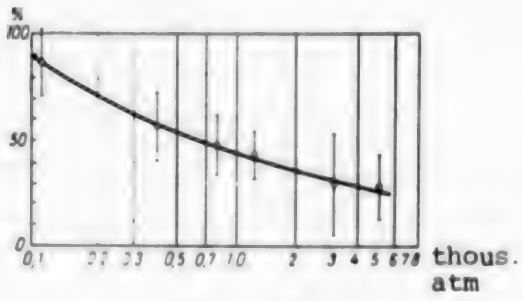

Figure 3.
Relative intensity of lettuce seed cell division as a function of pressure in impact wave-front

In Figure 2, there are 30-100 irradiated seeds and 20 swollen seeds at each pressure level. The striped band in Figure 2b shows the range of values for delay in start of seed germination in the control.

The impact wave has a noticeable effect on survival and delayed germination of dry seeds at 1000-2000 atm, and in the case of swoleen seeds this applies at pressure of only 200-300 atm. The impact wave also suppresses cell division effectively (see Figure 3): at 800 atm pressure, its intensity diminishes by about a factor of 2, as compared to the control. At the same time (see Table), we failed to observe noticeable increase in number of chromosomal aberrations. There were virtually no multiple chromosome aberrations.

Percentage of cells with chromosome aberrations in lettuce seeds exposed to impact waves of different amplitude

Parameter	Impact wave pressure amplitude, thous. atm						
	0.1	0.2	0.4	0.8	1.3	2.7	5
1st irradiation: Cells with chromosomal aberrations, %	1,17±0,52	1,65±0,62	0,58±0,24	0,67±0,38	0,92±0,38	0	2,4±1,7
Control	0,81±0,018, %						
2d irradiation: Cells with chromosomal aberrations, %	—	—	4,1±1,65	1,83±0,55	—	0	—
Control	1,54±0,41, %						

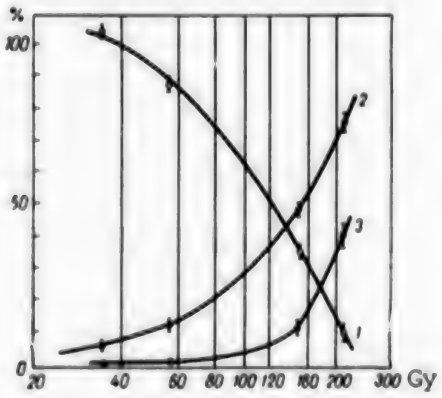

Figure 4.
Relative intensity of cell division (1), relative number of aberrant cells (20 and relative number of cells with multiple aberrations (3) as a function of dose of β-radiation delivered to salad seeds

We could refer to data pertaining to the effects of other types of radiation-- β-particles, protons, heavy charged particles--for better understanding of the specific effect of impact waves on biological systems. Pulsed irradiation using focused ultrasound may be the closest to an impact wave in nature of effect. According to data in [2], the effect threshold of pulsed delivery of radiation to various biological systems rises rapidly with decrease in pulse duration and increase in ultrasound frequency and, for example, if we were to extrapolate the data on destruction of deep structures of the rat and cat brain, which pertained to many thousands of atm at ultrasonic frequency of several megahertz and pulse duration of several tens of microseconds, i.e., a duration comparable to that of impact wave pulses used in our experiments. Thus, apparently impact waves are more effective in biological systems than pulsed delivery of focused ultrasound with short duration of pulses and low pressure amplitude.

To compare the specific effects of impact waves and ionizing radiation, we exposed air-dried lettuce seeds to β-particles from an $^{90}Sr+^{90}Y$ source in the dose range of 3.3-220 Gy. The results of exposing seeds to β-particles are illustrated in Figure 4. We failed to observe appreciable decline of survival rate following irradiation: even with delivery of maximum doses, all

of the seeds sprouted on the 7th day. However, there was appreciable depression of cell division, by about a factor of 2 with a dosage of 120 Gy. At the same time, with increase in dosage there was rapid increase in number of aberrant cells (from 0.3% in the control to 49% with 154 Gy). There were no cells with multiple aberrations in the control, whereas after exposure to radiation in a dose of 154 Gy they constituted 12%.

Data on the effect of heavy charged particles on lettuce seeds, which were obtained in experiments in space and with accelerators [5], indicate that there is an increase in aberrant cells and cells with multiple aberrations. In the case of long-term exposure of lettuce seeds in space, aboard Cosmos-1129 biosatellite and Salyut-6, seeds hit by heavy ions showed a noticeable increase in number of aberrant cells and cells with multiple aberrations. After exposing seeds to ^{4}He ions (energy 5.6 GeV, dose 170 Gy) on an accelerator, such cells constituted 54 and 23%, respectively. No depression of germination or intensity of germination of seeds was observed. After exposing seeds to protons (660 MeV, 5 Gy), aberrant cells constituted 5% and cells with multiple aberrations, 0.2%.

A comparison of the effects generated by an impact wave and ionizing radiation shows that impact waves with pressure amplitude of up to several thousand atmospheres elicit a decline in survival rate and intensity of cell division, but not to noticeable disturbances on the molecular level, whereas ionizing radiation, which does not have an appreciable effect on germination and energy of sprouting, depresses substantially the intensity of cell division, increases the percentage of aberrant cells and cells with multiple aberrations. This is related to the fact that impact waves at the pressure amplitudes used, unlike ionizing radiation, cannot transmit sufficient energy to the molecule to break intramolecular bonds, the energy of which may reach several electron volts.

Preliminary analysis of the effects induced by an impact wave passing through cells indicates that its action consists primarily of disrupting the spatial position and mechanical injury to different cell structures on the microscopic and submicroscopic levels and, to a lesser extent, on the molecular level. Obviously, the primary structural disturbances in the cell can not only suppress the intensity of cell division, but have far-reaching consequences with respect to vital functions and development of the cell, including its genetic mechanism.

Thus, analysis of the experimental results we obtained warrants the belief that some of the most sensitive biological microsystems can be injured by impact waves with pressure amplitude of tens of atmospheres which, according to our estimates, are present near the interface of the track of a heavy charged particle in a liquid medium.

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EFFECT OF STEROID HORMONES ON BIOGENIC AMINE LEVELS IN LUNGS DURING DEVELOPMENT OF PULMONARY HYPERTENSION IN RATS SUBMITTED TO CHRONIC HYPOBARIC HYPOXIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (manuscript received 15 Feb 86) pp 76-78

[Article by N. N. Pribylova]

[Text] At the present time, it is known that the lungs are involved in biosynthesis of phospholipids, coversion of angiotensin I to angiotensin II, metabolism of histamine, acetylcholine, kinins, prostaglandins, heparin, serotonin, catecholamines and vasoactive polypeptides [3, 11, 12, 14, 16]. There is information [5, 10, 13] to the effect that serotonin plays a part, not only in bronchospasm, but genesis of pulmonary hypertension. The pressor effect of serotonin on vessels in the pulmonary circulatory system is estimated as being 15-20 times stronger than that of epinephrine (E) and norepinephrine (NE). According to some studies [1, 4, 15], histamine is a mediator of bronchospasm and causes more marked constriction of pulmonary vessels than E and NE. Some researchers [8, 9] have shown that there is significant increase in E and NE content of blood and lung tissue in the presence of acute respiratory insufficiency.

Considering the close relationship between metabolism of steroid hormones and their effect on activity of biogenic amines, we undertook the task of testing the effect of steroid hormones on levels of the most important vasopressor amines (serotonin, histamine, E and NE) in lung tissue, in the presence of chronic hypobaric hypoxia.

Methods

Experiments were performed on 135 male albino rats weighing 120-200 g. Chronic hypoxia was induced in a hypobaric chamber, where animals were kept for 6 h/day at an altitude of 9000 m above sea level at a pressure of 220 mm Hg for 7 days, using the method of A. A. Birkun and I. N. Nemirovskaya [2], according to whom a model of pulmonary hypertension, cor pulmonale, is formed under such conditions.

The rats were divided into 10 groups, with 12-15 animals in each group. Hydrocortisone, testosterone propionate, progesterone in concentrations of 1 mg/100 g

weight and estradiol in a concentration of 0.1 mg/100 g weight were given by intramuscular injection to 4 experimental groups of animals, respectively, daily for 7 days. Twelve intact animals given no hormones served as a control for rats that were not submitted to hypoxia (4 groups of 12 rats each). In assessing the overall effect of hypoxia plus steroids on animals in the other 4 groups (15 rats in each), 15 control animals served for comparison; they were exposed to 7-day hypoxia but not given hormones.

E and NE levels in homogenized lung tissue were tested by the method of E. Sh. Matlina and T. B. Rakhmanova, which has been described previously [6]. Histamine and serotonin content of lung tissue homogenates was assyed by fluorimetry [7]. All of the tests on biogenic amines were performed on a spectrofluorimeter

Results and Discussion

The levels we demonstrated of tissue serotonin (2.66±0.11 nmol/g tissue), histamine (0.10±0.008 nmol), E (0.218±0.016 μg) and NE (1.24±0.29 μg/g tissue) in the lungs of intact healthy animals coincided with the norms cited in the literature [7, 9].

Levels of biologically active substances in white rat lung tissue in the presence of chronic hypoxia and under the effect of steroid hormones

Experimental conditions	Serotonin, nmol/g tissue	Histamine nmol/g tiss.	Epinephrine, μg/g tissue	Norepinephr., μg/g tissue
Control group (n=12)	2,66±0,11	0,107±0,008	0,218±0,016	1,24±0,29
Hydrocortisone (n=12)	2,05±0,22*	0,044±0,008**	0,485±0,010**	0,82±0,23
Progesterone (n=12)	2,02±0,21	0,053±0,007**	0,545±0,054**	0,41±0,05*
Testosterone (n=12)	2,78±0,45	0,046±0,003**	0,436±0,049**	1,89±0,35
Estradiol (n=12)	3,71±0,45	0,098±0,008	0,541±0,04**	1,47±0,35
Hypoxia in control animals (n=15)	6,58±0,45**	0,602±0,044**	0,442±0,010**	2,48±0,11**
Hydrocortisone + hypoxia (n=15)	0,22±0,05**	0,056±0,007**	0,453±0,043	1,35±0,29**
Progesterone + hypoxia (n=15)	3,17±0,51**	0,028±0,003**	0,453±0,027	1,65±0,23**
Testosterone + hypoxia (n=15)	3,23±0,28**	0,067±0,008**	0,47±0,016	1,06±0,17**
Estradiol + hypoxia (n=15)	3,91±0,34**	0,134±0,017**	0,48±0,27	1,41±0,35*

Note: Number of animals is given in parentheses.
*p<0.03, as compared to group of hypoxic control animals
**p<0.003

Analysis of data listed in the table indicates that, as a result of exposure to chronic hypoxia, there was significant increase in tissue serotonin and histamine content: 2.5-fold increase for serotonin and 5.5-fold for histamine. The level of tissue catecholamines underwent a 2-fold elevation. In the

experiments with reproduction of acute respiratory insufficiency [9], significant elevation of biogenic amines in lung tissue was demonstrated, with elevation of pressure in pulmonary circulatory system vessels, which no doubt confirms the role of biogenic amines in mechanisms of development of pulmonary hypertension. The results of our studies and findings of other authors [9] indicate that, in the presence of hypoxia, insufficiency of adaptation mechanisms is observed, which apparently depends on impairment of inactivating capacity of the lungs with regard to biogenic amines, primarily serotonin and NE.

It should be noted that the use of steroid hormones during 7-day chronic hypoxia elicited a marked inhibitory effect in the same direction on levels of vasopressor biogenic amines in rats--serotonin and NE (see Table) in lung tissue. The greatest inhibition was referable to serotonin formation in the lungs .... [segment missing in source] hydrocortisone. Steroid sex hormones had a moderate inhibitory effect on serotonin level in the lungs, particularly estradiol. A check of the effect of steroid hormones on intact animals without hypoxia revealed that estradiol elicited a tendency toward increase in serotonin concentration in lung tissue.

In the presence of chronic hypoxia and in parallel control tests without hypoxia, steroid hormones inhibited formation of histamine in the lungs. Hydrocortisone and progesterone had the maximum inhibitory effect, while estradiol elicited a minimal effect with and without hypoxia, under normoxic conditions.

We cannot rule out the possibility that it is expressly for this reason that, in response to giving estradiol, some animals presented regional moderate bronchospasm. A co-parison of experimental data to clinical studies of patients with bronchial asthma warrants the conclusion that hyperestrogenemia may play some role in provoking a serotonin and, to a lesser extent, histamine bronchospasm. However, one must bear in mind that strong antihistamine- and antiserotonin-neutralizing effect of progesterone on lung tissue in the presence of chronic hypoxia.

The extent of the effect of steroid hormones on catecholamine activity in lung tissue depended on individual distinctions of hormone action, and it was determined by normoxia or hypoxia. Under normoxic conditions, all steroid hormones increased E activity, which is an indirect indication of their involvement in synthesis of cycle AMP in lung tissue. However, during 7-day hypobaric hypxoia, steroid hormones did not lower E content, but did depress the concentration of NE, which has a vasopressor effect, which was largely instrumental in preventing development of pulmonary hypertension.

Thus, the above data are indicative of the important role of steroid hormones in metabolism of biogenic amines in the lungs under normoxic and particularly chronic hypoxic conditions. Administration of various steroids to intact animals had a dissimilar effect on levels of biogenic amines in lung tissue. Under normoxic conditions, all of the steroid hormones inhibited histamine and NE production in lung tissue. A maximum inhibitory effect was demonstrated for hydrocortisone and progesterone, but estradicl did not have such an effect. Under normoxic conditions, steroid hormones increased E content of lung tissue. Under hypoxic conditions, there is more intense release of tissue histamine, serotonin and catecholamines in the lungs. Formation of vasopressor

biogenic amines, which have a constrictive effect on pulmonary vessels, is decreased under the effect of steroid hormones. Inactivation of vasopressor biogenic amines in lung tissue under the effect of progesterone and hydrocortisone should be viewed as an important element in the pathogenesis and treatment of pulmonary hypobaric hypoxia.

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EFFECT OF INTERMITTENT HYPERCAPNIA ON VISUAL ANALYZER FUNCTION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (manuscript received 23 Aug 86) pp 78-80

[Article by T. I. Golubeva and M. P. Kuzmin]

[Text] Our objective here was to determine the response of man to increasing concentrations of CO_2 during long-term exposure to moderate hypercapnia. Heretofore, attention had been devoted mainly to the cardiorespiratory system and acid-base equilibrium in studies of man's adaptive reactions to high concentrations of CO_2 [3, 4]. Yet all of the body's adaptive responses to environmental factors are coordinated with the function of the nervous system, while its functional state directly determines human work capacity under such conditions. It is known that dark adaptation reflects not only processes occurring in the receptor proper, but are closely related to the optical centers of the cerebral cortex [2], and for this reason it can determine their functional state to some extent. We used the study of dark adaptation of the eyes as an indicator of the human body response to intermittent hypercapnia.

Methods

Functional state of the visual analyzer was examined on 4 subjects on specific days of their 40-day stay in an atmosphere with 1.3±0.1% CO_2. During this long-term exposure to hypercapnia, CO_2 content was increased twice to 4%. The first increase was made in 24 h by the 22d day and the second in 48 h by the 39th day. The 4% concentration was maintained for 48 h and reduced in 2 h. Dark adaptation of the eyes was measured at 1600 hours using an ADM adaptometer by the 3-min method. We determined the time between end of deadaptation (light flashed for 2 min, 795 cd/m^2) and moment when the subject noticed the test object. The eyes were examined, ophthalmoscopy performed and intraocular pressure was measured before and after this test.

Results and Discussion

During a long-term stay in an artificial atmosphere with 1.3±0.1% CO_2, the subjects presented phasic changes in visual analyzer function. The rate of dark adaptation fluctuated over a rather wide range. Analysis of mean values for this parameter (see Table) indicates that there is adaptation of the visual

Dark adaptation time in hypercapnic atmosphere (M±m)

Parameter	Day						
	3	6	8	10	12	15	17
CO_2 concentration, %	1,5	1,3	1,4	1,4	1,3	1,3	1,3
Time, s	64±17	97±29	93±27	43±7	95±6	72±16	85±23

Parameter	Day						
	22	25	27	30	32	35	39
CO_2 concentration, %	4,0	1,4	1,3	1,3	1,4	1,4	4,0
Time, s	115±19	60±18	64±23	28±6	66±28	58±18	88±43

analyzer to prolonged moderate hypercapnia. When the CO_2 concentration was raised to 4% on the 22d day of the study, all subjects presented a reaction in the same direction: significant increase in dark adaptation time.

It should be noted that dark adaptation time diminished reliably ($p<0.05$) to the baseline level and was notable for rather high stability after lowering CO_2 content in the atmosphere to 1.4% on the 25th day of the study. Thus, relatively brief elevation of CO_2 level to 4% during moderate hypercapnia elicited a strain on compensatory mechanisms and led to increase in dark adaptation time.

The second increase in carbon dioxide content to 4% on the 39th day of exposure to a hypercapnic atmosphere caused significant slowing of dark adaptation in only 2 subjects, whereas in the other 2 this parameter did not change. For this reason, the mean value for this parameter was noticeably lower than on the 22d day, in the period of the first increase in CO_2 content. Thus, the nature of changes in response of the visual analyzer to repeated exposure to high concentration of CO_2 was more moderate, and this could be related to slower rate of increase in carbon dioxide [1].

Ophthalmological examination failed to reveal any deviations from the norm in the eyes of the subjects in the baseline state. Right after 40-day exposure to a gas atmosphere with high CO_2 content, all of the subjects showed an increase in density of the eyeballs upon palpation. Intraocular pressure was at the top of the normal range (28-29 mm Hg), and in 2 cases it was above normal (33 and 31 mm Hg). Ophthalmoscopy revealed moderate dilatation of arterioles and veins of the retina in all subjects. There was no change in visual acuity.

Studies of functional state of the visual analyzer during intermittent exposure to a hypercapnic gas atmosphere revealed that the parameters under study reverted to the baseline level after brief increase in CO_2 concentration to 4%. Our findings are indicative of adequate compensatory capabilities of the eye's vascular system, providing for the function of the human visual analyzer.

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MONONUCLEAR PHAGOCYTES DURING ADAPTATION OF ESSENTIALLY HEALTHY PEOPLE TO HIGH ALTITUDES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (manuscript received 3 Mar 86) pp 80-82

[Article by M. I. Kitayev and A. G. Goncharov]

[Text] The mononuclear phagocyte system (MPS) of essentially healthy people has not been discussedin the literature as it pertains to adaptation to alpine regions. Yet, these cells perform important functions in the body. They are involved in granulopoiesis, synthesis of biologically active substances and regulation of the immune response at all of its stages [4, 5, 9, 10, 13]. It can be assumed that the MPS is involved in maintaining immunological homeostasis in naturally occurring hypoxic environments. Our objective here was to investigate the functional distances of blood monocytes during man's adaptation to the altitude of the Pamir region.

Methods

Evaluation of the MPS involved examination of the monocytogram according to O. P. Grigorova [2] and phagocytic activity of blood monocytes with latex particles, determination of EAC [erythrocytes sensitized with antibody and complement]-rosette-forming monocytes for demonstration of receptors for the C3 fraction of complement and EA-rosette-forming monocytes for demonstration of Fc receptors of immunoglobulins on the membrane [8].

We examined a group of 51 male volunteer subjects 18 to 22 years old. The study was pursued in three stages. Baseline studies were conducted at an altitude of 1543 m above sea level, then on the 3d-5th and 25th-30th days of adaptation to 3600 m above sea level. The altitude gradient was 2057 m. After the ascent, the subjects were divided into two groups: the 1st consisted of 33 men with good adaptation process and the 2d, 18 men who developed acute mountain sickness (AMS). The diagnosis of AMS was made on the basis of the typical clinical signs and was considered reliable if the AMS symptoms persisted for 3-5 days or longer. In addition, we examined 20 men 22 to 44 years of age who were born and lived at an altitude of 3600 m above sea level.

Results and Discussion

On the first days after ascent, healthy subjects with good adaptation process presented insignificant increase in both absolute and relative monocyte

content, which dropped dramatically by the 25th-30th adaptation day without, however, dropping to the level demonstrated in the indigenous mountain residents. Monocyte level did not undergo significant change in the adaptation period in those who developed acute mountain sickness. The monocyte count of subjects with AMS was considerably lower in the baseline period ($p<0.05$) than in those without deadaptation pathology (Figure 1).

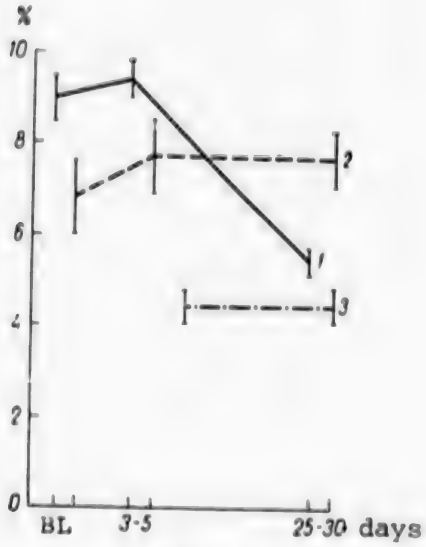

Figure 1.
Monocyte level in subjects with good adaptation (1), AMS (2) and indigenous mountain residents (3). Y-axis, monocyte level (%)
Here and in Figures 2-4):
BL) baseline
X-axis, day of adaptation

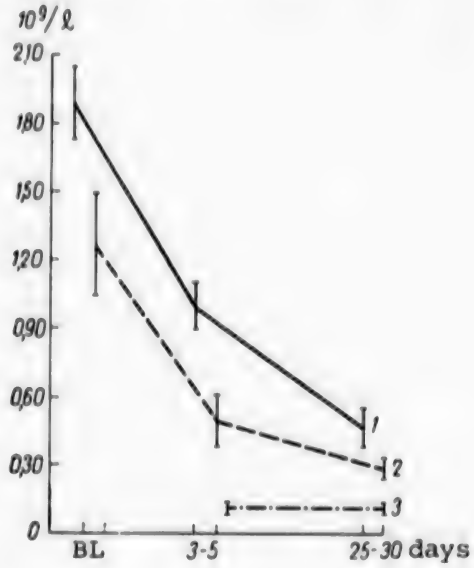

Figure 2.
Level of monocytes phagocytizing latex particles in subjects with good adaptation process (1), AMS (2) and indigenous mountain residents (3). Y-axis, number of phagocytic monocytes ($\cdot 10^9/\ell$)

Examination of monocytograms revealed that proliferative processes underwent changes in the same direction in both groups: they were more intense by the end of month-long adaptation. Analogous changes also occurred in the differentiation index.

In the course of the study, both groups of subjects revealed dramatic decrease in number of phagocytic monocytes (Figure 2) in accordance with duration of stay at high altitude ($p<0.05$). Typically enough, at all stages of our study this parameter was higher with statistical reliability in the group with good adaptation process than those with deadaptation pathology. In addition, in spite of the significant decline in number of phagocytic cells in healthy subjects, by the end of a month's stay at high altitude this parameter remained higher ($p<0.05$) than in local residents. At the same time, the mean number of latex particles consumed per monocyte diminished insignificantly in the course of adaptation. Thus, in the course of adaptation to high altitude there is a decrease in number of actively phagocytic monocytes.

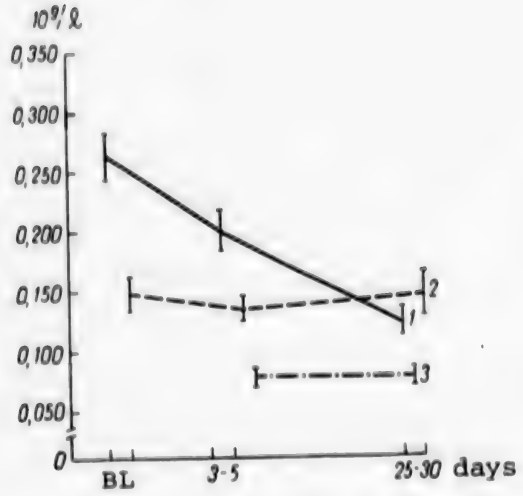

Figure 3.
Level of monocytes forming EAC rosettes in subjects with good adaptation process (1), AMS (2) and indigenous mountain residents (3)
Y-axis, number of EAC-rosette-forming monocytes ($\cdot 10^9/\ell$)

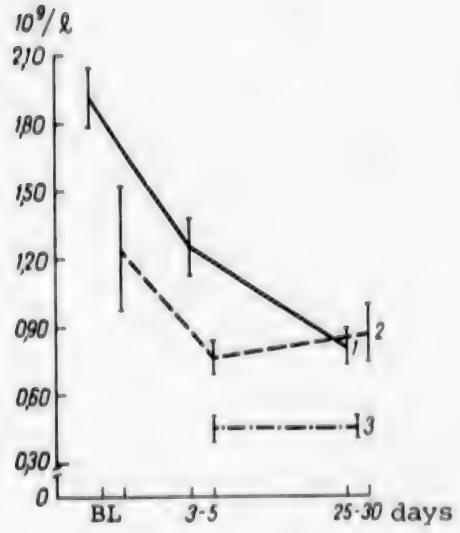

Figure 4.
Level of monocytes forming EA rosettes in subjects with good adaptation process (1), AMS (2) and indigenous mountain residents (3)
Y-axis, number of EA-rosette-forming monocytes ($\cdot 10^9/\ell$)

To effect immune phagocytosis, monocytes have receptors on their surface for the Fc fragment of immunoglobulins and C3 fraction of complement. In the course of our study we found that there is a decrease ($p<0.05$) in relative number of monocytes with C3 and Fc receptors in healthy subjects on the 3d-5th day in the mountains, whereas by the 25th-30th day it increases without, however, reaching the baseline ($p<0.05$). It must be noted that the absolute number of such cells in blood diminished throughout the month-long adaptation (Figures 3 and 4).

In subjects who developed AMS, we observed a decrease in absolute and relative number of EA-rosette-forming monocytes (see Figure 4), whereas the level of EAC-rosettes showed virtually no change (see Figure 3). It is important to note that the number of rosette-forming cells was reliably higher in the baseline period in the group of healthy subjects than those who developed AMS. In addition, the number of monocytes with Fc and C3 receptors on their surface remained higher after 1 month in the mountains than in the indigenous subjects ($p<0.05$).

Thus, with adaptation to mountain altitudes, there is a decline in functional activity of monocytes. On the first few days after ascent, there is a decrease in number of monocytes forming EAC- and EA-rosettes, whereas by the 25th-30th day, in spite of some increase, it does not reach the baseline level, which is indicative of depression of MPS cells.

Typically enough, the mononuclear parameters of subjects with AMS were lower at all stages of the study than in those with good adaptation process. In addition, on the 25th-30th day in the mountains, these parameters were statistically higher in healthy subjects than in the indigenous subjects. Perhaps, this is related to the age-related differences between the mountain residents and our volunteers.

The described changes in the mononuclear phagocyte system should apparently be related to the effect of the set of mountain altitude factors, the principal one being the low partial oxygen pressure, which leads to development of hypoxemia and hypocapnia that have an adverse effect on nervous and humoral regulation [1, 6, 7, 12]. The rise in corticosteroid content of blood with adaptation to high altitude [3] perhaps also has an adverse effect on MPS cells, since according to A. Fauci [11] corticosteroids have a suppressive effect on the subpopulation of mononuclear phagocytes.

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BOOK REVIEWS

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NEW U.S. BOOK ON AVIATION PSYCHOLOGY REVIEWED

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[Review by A. A. Gyurdzhian, V. F. Tokarev and Yu. Yu. Shipkov of book, "Aviation Psychology," by S. N. Roscoe, Iowa State University Press, Ames, 1980, 304 pages]

[Text] S. N. Roscoe is a professor of pscyhology, chief of the engineering psychology laboratory at the University of New Mexico and head of the Illinois School of Aviation Psychology. He has had some experience as a flight instructor and transport pilot in the U. S. Army.

The book consists of a foreword, 6 parts (24 chapters) and appendices, which include a list of abbreviations, brief glossary, extensive bibliography (about 350 references), subject and author indexes.

There are 17 U. S. specialists who co-authored different chapters. The participation of S. N. Roscoe as author in all (but one) chapters has resulted in a monographic and standard style of presentation.

The following quotation of Professor U. S. Hunter was chosen as one of the epigraphs: "If there should be another war, the victor will not be the side that has the most powerful troops or even the side that has the most accurate missiles, but the side that will be at least 10% better in solving vital problems of the human factor."

The history of aviation psychology in the United States, basic concepts of aviation psychology, directions and prospects of its development are covered in the foreword and first part of the book (Chapters 1 and 2). The professional performance of a pilot is submitted to psychological analysis.

In the second part (Chapters 3-8), there is discussion of the main guidelines of engineering psychology and their practical application to the design of information display systems and controls.

The rapid development of aircraft engineering has posed the acute problem of studying pilot performance and improving his efficiency in a pilot-aircraft system, particularly with respect to his processing of extensive and diverse

information. Advances in computer technology are helping solve the problem of optimizing interaction between pilot and aircraft. It should be conceded that, at the present time, the information received by a pilot is far from being adequate for piloting requirements, particularly for nonstandard flights. The task for designers and psychologists is to provide the optimum time and space correlation between the readings of different instruments, information about needed and actual flight parameters, pilot operations to control the aircraft (choice and execution of control actions) and the aircraft's responses to the latter. In the opinion of A. K. Williams (author of Chapter 2), pilot performance can be conceived as the combined operation of a computer (when a pilot decides what to do) and servosystem (when the pilot compares the expected and actual results of his actions).

A proper relationship between solving basic and ancillary flight problems is an important element of pilot work. The book offers the following hierarchy of principal and ancillary tasks put to a pilot.

1. What is the route to his destination and what is the location of the aircraft in relation to the route and destination?

2. What should the velocity vector be and what is it in reality?

3. What should be the aircraft's position, engine thrust, flight trajectory, and are they in reality?

4. What action should be taken with the controls to eradicate the discrepancy between specified and actual parameters?

Aircraft controls: It is only since the start of the 1970's that steps were taken to improve different control levers to optimize their kinematics. However, evolution of the aircraft in space, with consideration of six degrees of freedom, depends on the complex interaction between several controls, aerodynamics, velocity and trajectory of flight, meteorological conditions, amount of fuel, stage of flight and many other factors. In this respect, refinement of the aircraft control system and development of integrated systems that consider all factors constitute a priority task. It can be stated that refinement of control systems is lagging, in relation to development of information display systems.

Optimum distribution of functions among automatic systems and the pilot, among automatic, semiautomatic and manual forms of aircraft control, and optimum distribution of functions among crew members constitute the most important objectives in control data display systems.

Integrative systems of data display and various types of displays which submit data in parametric, graphic and dialogue forms, have been proposed. Various classifications have been offered for displays that exhibit information about the situation in the vertical and horizontal planes, in front, behind and under the aircraft; there is discussion of displays that are situated on the forward transparent surfaces and on the pilot's helmet. This sections ends with a discussion of systems of information display and controls. The rapid advance of aviation technology, great specialization of types of aircraft and their

purposes have led to excessive diversity of systems, which makes it difficult to train flight personnel and retrain them for new equipment. All this puts the task to designers of developing unified, synthesized and flexible multi-purpose systems.

Much attention in the book is devoted to questions of optimizing display of information that enables the pilot to promptly predict changes and maintain the required flight parameters. It submits the results of relevant research on optimization of instruments showing the dynanics of changes in flight velocity and altitude (of the rate-of-climb indicator type), investigation of factors affecting efficiency of pilot tracking performance and to determine the role of various segments of the retina in perceiving instrument information.

There is then discussion of the urgent question of optimum correlations between actual change in the aircraft's position, change demonstrated by the instrument and direction of movement of the control required to return the aircraft to the proper attitude.

It is important to spatial orientation of the aircraft that there are two system of coordinates: ground and aircraft. There has been a debate for a long time about what the instruments (for example, the gyro-horizon) should show: the aircraft's attitude in relation to earth's coordinates or the position of the horizon in relation to aircraft coordinates? What is considered the background and what, the moving indicator figure? With regard to brief perturbances and changes in the aircraft's attitude, it is desirable for instrument readings to be analogous in direction of human perception of corresponding accelerations by means of sense organs ("kinanalogue" principle, i.e., kinesthetic analogue). This provides for an adequate relationship between instrument readings and direction of corrective controlling motion. For the slow component, which shows the aircraft's attitude, a different display principle is desirable. Both signals can be differentiated by means of special frequency filtration.

The facility of training young aviation school cadets and pilots being retrained on new equipment are criteria of the effectiveness of different systems of displaying information about flight parameters. However, it should be borne in mind that the effectiveness of some system depends more on a pilot's experience, difficulty of the flight assignment and many other factors.

The problem of generalized synthesis of the information display system and control system with extensive use of computers is discussed at the end of the second part of the book. There is discussion of the analytical approach to problem solving, integrated and graphic display of information, various levels of control actions, in which compensatory and pursuit tracking is used, prediction and anticipation of perturbations, as well as practical application of these guidelines under different conditions and with different types of flights.

The third part of the book (Chapters 9 and 10) deals with some perceptual phenomena of flight work.

There is a rather interesting description of some optical illusions, in particular those related to mutually determined subjective estimates of distance to some object and object size. Both estimates depend on eye accommodation at a given point in time. These illusions may be the cause of or instrumental in

aviation accidents, particularly at the landing approach and landing stages under adverse weather conditions. For this reason, the author deems it desirable, in screening pilot candidates, to take into consideration the individual distinctions of eye accommodation at rest in the absence of any objects in the field of vision (empty space myopia), i.e., individual distinctions with respect to distance at which the eyes focus under such conditions. Special conditioning of the visual system of flight personnel is probably very important in this respect. One of the possible means of preventing such illusions is to wear bifocal glasses, in which the bottom part of the lens has greater refraction for reading instruments on the instrument panel which is close to the pilot and the top part has less refraction for visualization of distant objects outside the cabin. Various optical devices have been suggested to monitor instruments without appreciable eye accommodation, which could elicit an illusion with a sudden glance toward the outside space.

A rather interesting phenomenon caused by oculomotor-vestibular interaction, which is important from the standpoint of flight safety, is closely linked to the above-mentioned optical illusions. This phenomenon is described in the fourth part of the book and consists of the following. Exposure to intense rotation, as well as many other factors that induce stress (in particular, a dramatic pressure gradient), can in some cases cause hyperaccommodation of the eyes (focal distance is reduced to 1 m) for one or several minutes. The dimensions of objects projected on the retina from distant (outside the cockpit) space are perceived as being smaller than in reality; when landing, the pilot flies over the glide path at a higher altitude and touches down farther than he should.

This part of the book also discusses problems of display of information obtained by means of radar, infrared and electron-optical probing. We refer to methods of improving efficiency of target retrieval, possibility of distinguishing a moving target from backgroun and artefacts, choice of optimum contrast between the image and background. In order to obtain good results in this respect, one has to vary the time and space characteristics of the field of vision, superimpose several images and distinguish between seeming motion and actual movement. The results of relevant studies are submitted, in particular those dealing with tracking of artificial earth satellites and objects of subliminal intensity.

The fourth part of the book (Chapters 11-14) deals with evaluation of individual tendencies and abilities of flight personnel, their work capacity and quality of performance of their work.

It was shown that it is possible to predict flight skills and achievement of secondary school graduates and first-year flight school cadets. It is difficult to differentiate the individual skills of different people when performing a standard work load. More complicated and additional tests are needed, in particular to detect the ability to distribute attention. Regular and long-term studies must be made of the flying careers of tested groups in order to elaborate and check the validity of tests, criteria and operational tasks put to pilots in order to predict their abilities. Airline companies, which test pilot performance every 6 months, have accumulated some experience in this respect. However, the formal legal restrictions do not permit use of these checks of flight personnel in the way required in the interests of the problem.

A method involving concurrent performance of two or several tasks is used for practical evaluation of an individual's capacities, in particular, for flight work. A list is offered of exogenous and endogenous factors that affect test achievement. It is very important for the test results to be independent of individual experience, knowledge and professional training. There is discussion of the elements in the test performance process: perception of signal, its recognition, processing, human responses and storage of information in memory. So-called "transformation," the purpose of which is to correct the direction, program, velocity and amplitude of the response, is an additional element. There is discussion of the tracking method, set of North-Hofer cues and its modification made by North. The flaws of these methods are noted, and analysis is made of the prospects for using them to screen specialists in other fields.

Methods of reliable and objective monitoring of a pilot's actions in flight, criteria of quality of performance of flight elements, mistakes made by the pilot, methods of generalization and analysis of results are of considerable interest. All this is necessary to derive an expert conclusion, promptly correct cadet instruction and refine the organization of flights.

Three interrelated concepts are discussed: work load, attention span and pilot errors. The rules of air navigation were made on the basis of the range of permissible random errors and deviations of pilot actions. Among the numerous factors determining flight incidents, control of the most significant ones will, of course, yield the most noticeable positive effect. For example, 25% improvement in flying precision as a result of refinement of data display and control systems results in 100% simpler operation of the onboard computer. This means that control of pilot error is the most important objective. But how is one to measure the probability of pilot error and reduce it as related to refinement of flight equipment and techniques? How can we relate the results of laboratory tests on simulators to actual flights? These questions are attributable to the difficulty of measuring the pilot's work load, difficulty in determining the probability and frequency of pilot error under different flying conditions and with use of different equipment and navigation systems. Apparently, measurement of the pilot's inflight attention span is a promising approach. To illustrate these theses, examples of flight incidents are cited in the book. There is convincing argumentation of the thesis that the term, pilot error, is unfortunate, since it does not help disclose the true causes of pilot actions that are inconsistent with the design of the aircraft. As a last resort, one could refer to "piloting error."

In the fifth part of the book (Chapters 15-22), there is discussion of different aspects of pilot training.

In the United States, there are about 1 million pilots. We were impressed by the wide diversity of flight personnel teaching methods, which depend on the individual distinctions of the instructors. Standardization of teaching methods should be based on thorough understanding of the functional "pilot-aircarft" model. A distinction can be made between three elements of flight work: operational, the one related to decision making and the perceptual-motor element. These concepts are described in the book.

We can assess the effectiveness of the current program of flight training from the generalized figures referable to flight accidents in the United States. In 1976, 0.0002 death/million passenger-km were recorded on the regular airlines, 0.2765 in the general aviation and 0.0331 in motor vehicles.

Of the total number of flight accidents without fatalities, 57.2% were the pilot's fault and caused by errors of perceptual-motor origin (failing to maintain the proper distance, altitude, speed, etc.), whereas in 50.4% of the cases the cause of catastrophes (i.e., accidents with fatalities) was referable to incorrect decisions (visual flight under difficult weather conditions, improper planning and preparation for flight). A combination of unfavorable individual psychological traits, difficult inflight situation and flaws in pilot training is most often the cause of a flight incident that is the pilot's fault.

The authors of the book believe that the current system of pilot training is strictly empirical and has no theoretical foundation. It is necessary to do much work with instructors in order to standardize methods of training flight personnel. In-depth investigations must be made of the question of which skills and to what extent they are transferred from a simulator to actual flight in order to make successful use of simulators and mock-ups in flight training. Questions of flight training must be resolved in conjunction with other problems of development of aviation.

Flight instruction, like any other, should be so designed as to have each successive phase facilitated by the preceding one. This is the basis of recommendations to use previously learned elements in the next phases. A comparison of the effects of training in an experimental and control (without prior instruction) groups permits determination of the transfer (use) of previously acquired skills. The authors make a distinction between "cumulative" and "incremental" (growing) effectiveness of transfer. The mathematical system of relevant calculations, economic gain and corresponding strategy of instruction, as well as different factors affecting efficacy of training are furnished. The views that are expounded are relevant not only to determination of an economically advantageous program for moving from different types of simulator training to actual flight, but to other types of instruction.

There is discussion of the economic expedience and effectiveness of ground-based flight simulators. The possibility of acquiring skills on a simulator that are transferred to practical flying with a positive or negative sign, stages of instruction when simulator use is particularly effective, as well as comparative cost of simulator and actual flight training are discussed. Thus, the strategy and program of combined simulator and flight training are being developed for different stages of this process, different aircraft and for the performance of different flight assignments.

The question of status of simulator development is discussed. It is difficult to offer the basic specifications for simulators. It is logical to strive to develop simulators that imitate flight conditions the most. Ideally, it would be an aircraft in flight. However, refinement of ground-based simulators requires much expense. For example, to double the duration of exposure to accelerations all of the linear dimensions of the simulator must be enlarged 8-fold, while the space for its installation must be 512 times larger. There

is particular increase in indirect expenses (for energy, life-support system, visualization system), as well as design and manufacture. Perhaps it is particularly difficult (or impossible) to develop a perfect visualization system to teach skill in decision making under visual flying conditions.

When selecting a simulator, it should be borne in mind that acquisition of skill in piloting a mobile simulator does not yet indicate that this skill will be transferred to an aircraft and facilitate its control. Being synthetic (complex), simulators must be inexpensive since by conception they are intended to replace only a few hours of flight aboard small aircraft.

More expensive simulators can be developed for large and expensive aircraft. For example, a 1-h flight aboard a Boeing-747 costs $4000, whereas the cost of a simulator for it is $400. It is desirable to use simulators in training for solo and visual flights, when relearning to pilot new equipment, learning to land in the presence of turbulence and cross-winds, as well as air-to-air and air-to-ground combat.

Experience in flight training (in particular, retraining) shows that the most difficult problems are encountered when acquiring cognitive skills. Motor skills for control of all types of aircraft have rather much in common. For this reason, it is necessary to update simulators and have them conform to the newest aircraft models.

There is discussion of the possibility, effectiveness and expediency of using mobile simulators for flight personnel. Of course, there is the desire to reproduce in them, as much as possible, the dynamic conditions of flights, including feedback from the results of the pilot's controlling actions. However it is virtually impossible to simulate many of the dynamic conditions.

Simulators are used for research purposes, expertise and flight training. The first two aspects do not, of course, raise any particular questions. As to the third, a significant number of studies have been conducted. Their main result, in the opinion of the book's authors, is that mobile simulators do indeed facilitate training and yield better results than stationary ones. In essence, such results are attributable to the fact that the student acquires skill in relying on instrument information, in spite of movement of the cockpit. However, the great expense of developing particularly complicated mobile simulators is hardly desirable, since there is virtually no manifestation of a positive effect of these additional features on the learning process.

Specifications that must be imposed on the system of visualization and visual reference points in simulators designed for instruction in flying with direct visual control (particularly when making a landing approach and landing) merit investigation.

Development of computer engineering has offered many possibilities for reproducing in a simulator different visual situations. At the present time, there is a significant number of visualization systems differing in complexity and cost.

The problem is to determine the extent to which the visualized situation should show deails of the actual one. While it was previously believed that the more detailed the picture of the situation, the better, at the present time much doubt has arisen on this score.

A special taxonomy was developed of the characteristics of visual reference points and objects (text, color, volume of visual information), means of displaying them, role in different situations. The problem of conformity of information to psychophysiological characteristics of the pilot, as well as conformity of information to the experimental task or purpose of training, are discussed.

It is a difficult task to make the proper choice of the most important visual landmarks and extent of details about the situation. It should be noted that there is a certain optimum level of details in the observed picture, below and above which the training results are poorer. Choice of the most important reference points and objects for their visualization can be made on the basis of theoretical premises or special research. However, the latter is rather time-consuming, since it is then necessary to compare values of many factors and their combinations. Moreover, the conclusions derived from this work are referable to simulator training, and they indicate nothing at all about transferring the acquired skills to an actual flight.

The question of most effective use of visual landmarks, their choice and selective amplification is very important in training cadets on simulators with visualization of the situation, especially during a landing. The history of development of simulators with different types of visualization is descirbed; questions of proper display of visual information that is of greatest importance for making a landing approach and landing are covered: horizon, structure of the earth's surface, demarcation of runway, its axial line, aiming and contact points. Proper tactics in this respect helps develop the necessary skills, in particular, in visual scanning during a larding.

Not only proper choice of the most relevant visual reference points, but their amplification and delivery of additional information are very important to successful training in landings. The result of controlling actions, in the form of feedback, is exhibited to the operator in the form of visual information on a display or in the form of tactile stimuli. Both the desirable parameters and actual ones can be shown on the display simultaneously, or else the signal is delivered when some parameter exceeds permissible deviations.

The principle of an adaptable simulator involves immediate elimination of excessive (as compared to actual) and additional information as the appropriate skills are acquired. In addition, the adaptable simulator makes it possible to submit to the operator a set of information that conforms to his individual distinctions and stage of training.

All of the above theses and conclusions of the book's authors are based on concrete original research, with consideration of expenses and time, and there are provisions for transferring the skills acquired with use of the simulator to actual flights in aircraft.

Adaptive perceptual-motor training should be pursued on an individualized basis with gradually increasing complexity of tasks in accordance with stage of acquiring skill. One can facilitate the tasks at the first stages of training by, for example, using simpler control actions, shorter interval between the controlling action and its result, excluding dynamic interference, etc. It is only important to reach the required level as a result of instruction. Thus, relatively inexpensive simulators with a flexible program could be more beneficial than expense and complicated ones, presuming to copy exactly a real situation.

Special investigations revealed that better results are achieved on a ground-based simulator by the adaptive training method (proceeding from simple to difficult tasks) than with immediate training in a complicated task on a full program (control group). As for transfer of acquired skills to an actual flight in an aircraft, evaluation of the results is somewhat more complicated. They are better in those trained by the adaptive method than in the control group in some of the cases and worse in others. A series of other studies also failed to demonstrate advantages of the adaptive training method, for example, experiments where the order of operations was varied and the result of controlling action was deferred.

Thus, the negative results of using the adaptive method seem to contradict the well-known didactical principle of "from the simple to the difficult." The entire question lies in how to separate a complicated task into simple ones.

Whatever the algorithm of the task to be performed with the adaptive training method, the cadet always solves a similar problem: he maintains the signal parameters on the display (feedback) within the specified range. This is probably the cause of negative results. Apparently, an acquired simple skill must become a natural element in a more complex algorithm of operations.

Only one fact is unquestionable: intensified feedback (if the natural signal is weak) from the most important parameters, as well as specially selected ancillary signal-reference points, being adaptively controlled in the course of training (we are referring to their attenuation and exclusion as the relevant skill is acuiqred), are instrumental in learning and transferring acquired skills to an independent aircraft flight. Thus, the principle of adaptive training automatically provides for a constant optimum level of learning difficulty all of the time. But it is not only a matter of constant level of difficult. Much research work is needed to select the most important signals, logical order of complicating the tasks in order to achieve enhancement, potentiation of an acquired skill, rather than simple transfer of this skill. In all cases, economical estimation is a true compass when selecting the most effective training system.

The wide use of computers for development of a system of automatic programming of adaptive training will make it possible to better investigate the formation of perceptual-motor skills.

However, one should not exaggerate the role of computers as substitutes for instructors. Computers merely help and add to the utterly unique work of instructors.

The book then goes on to discuss the role of computers in flight training and a number of didactic aspects of flight training, for example, the relationship between theoretical instruction and various stages of practical assimilation of flight skills in simulators and training aircraft, prospects of introducing computers at all stages of flight crew training, in particular, in learning radio navigation methods.

Use of computers reduces the cost and time of instruction, brings closer to reality the content of problems solved in the training process, and brings us closer to adhering to the guideline of "on the job training." It is important that computers provide for an enormous range of problems dealing with preparation and planning of a flight, with due consideration of all the numerous factors and variants. Computers offer vast opportunities, not only for informational training, but to acquire skill in piloting an aircraft and making decisions in a changing, nonstandard situation, including air combat conditions.

It remains to be added that the use of computers (programmed training) provides beneficial opportunities, not only for direct training, but for periodic testing of its efficacy, making corrections in this process, as well as for conducting tests.

Thus, computerization of flight training has a great future.

Finally, the fifth part of the book, which consists of two chapters (23 and 24), sheds light on some of the results of special investigations.

One can follow the evolution of operational systems and the systems analysis approach by studying modern aviation systems that are functionally so complex that one cannot make any improvements in them by the trial-and-error method. For this reason, a safe, reliable and economical strategy must be elaborated to refine complex equipment and organizational forms of work. The basic concepts and definitions are offered for such terms as "operational system," "human engineering (engineering psychology," "systems analysis approach," "systems engineering," "systems design," "systems analysis," "systems synthesis," "systems evaluation (expertise)," etc. Systems analysis, synthesis and evaluation are elements of a single process of system evolution.

Then there is discussion of the advantages of using the systems method to organize air traffic control, conduct research (with consideration of numerous limiting factors) with optimum and mutually complementary distribution of functions among man and machine.

The last, 24th chapter has a somewhat unusual title: "Galileo and the Commercial Director." It discusses the methodology of research in aviation psychology, starting with the onset of some problem (by observation, formation of hypothesis, organization of studies, consideration of numerous attendant factors, analysis of results, deriving conclusions) to practical introduction and theoretical generalization. Galileo's investigation of the travel of cannon bullets yielded, as we know, very much to the formation of ballistics, and it is an example of logical construction of an investigation. It is more difficult for researchers dealing with extremely complex aviation equipment

systems that have numerous variables. It is even harder for those who study behavioral reactions of living things and particularly man in man-machine systems. Here, along with physical factors, one has to consider biological, social, psychological and legal ones.

Some interesting examples are cited of how failure to consider some factor that seems insignificant at first glance concealed the truth from the researcher in human engineering studies. A successful human engineering solution has a large economic effect. In particular, research is discussed, in which an additional work load and having an operator solve an extraneous problem disclose his residual attention capacity. The significance of proper definition of the priority and hierarchy of tasks is stressed. Modern experimental installations and methods of statistical analysis (for example, improvement of the effect of operating radar systems obtained with use of certain elements of man's perceptual systems) afford vast opportunities for human engineering reserach and refinement of engineering systems.

However, all this is only the visible tip of the iceberg, since the amazing time-and-space integrative processes of the brain constitute infinite reserves for use in engineering and ergonomics.

The following logical sequence formulated by Northrop is recommended by the author of this chapter to make use of them: disclosure of theoretical roots of the problem; choice of simple and vivid phenomena indicating the factors involved; observation of these factors; formation of appropriate hypothesis; derivation of logical corollaries of the hypothesis; determination of the primary problem in the light of the confirmed hypothesis; generalization of the solution obtained to the problem, application of new conception to practice.

The book being reviewed deals with the ergonomic aspects of modern aviation. In this respect, the book makes a good impression because of its practical aviation orientation. This is achieved, in particular, by the fact that the author chose not to use the usual chapter headings inherent in manuals of psychology, and took as his basis the logic of ergonomic investigations and simulator training of flight personnel. Prob'ems of developing new integrative information display systems and controls, with due consideration of a number of interesting motor-perceptual phenomena, are covered in sufficient depth and on a modern level. We were particularly impressed by the chapters dealing with specifications for new simulators, where the authors stress the need for making them more complicated to a specific degree, having them reproduce the dynamic conditions of an aircraft cockpit and visual situation. Chapters covering the strategy and tactics of combining various forms of simulator training and instruction during real flights in aircraft are important. There is detailed discussion of the possible methods of assessing the process of acquiring flying skills at different stages of training and effective transfer of acquired skill from one training stage to another.

Most of the expounded theses are based on analysis and comparison of the results of special model, simulator and flight studies conducted by S. N. Roscoe et al., as well as other representatives of the Illinois School of Aviation Psychology, which is quite interesting from the scientific and practical points of view.

Finally, there is another remarkable feature in the book, in particular, in the section dealing with simulator and flight training. All of the lay-outs concerning tactics of combining simulator and flight training are based on meticulous and comprehensive economic-financial calculations.

The book is of definite interest to specialists in aerospace medicine, psychology and ergonomics, flight trianing methodologists and aircraft captains, engineers and designers of information display systems, controls and simulators.

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NEW BOOK ON SPACE ECOLOGY REVIEWED

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[Review by V. P. Pishak of book, "Kosmicheskaya ekologiya" [Space Ecology], by V. G. Sidyakin, N. A. Temuryants, V. B. Makeyev, and B. M. Vladimirskiy, Kiev, "Naukova dumka", 1985, 176 pages]

[Text] In recent years, it has been inherent in ecological science to strike roots in new areas of research. It has become full of new content. The book being reviewed deals with pressing problems: effect of space on earth's ecological systems and wise environmental protection.

The monograph, "Space Ecology," consists of an introduction, five chapters and appendix. It contains 24 tables and 59 illustrations. This collective work is based on the results of many years of reserach conducted by N. A. Temuryants on the effect of space factors on peripheral blood, the work of V. M. Vladimirskiy on effects of solar activity factors on warm-blood animals, microorganisms and investigation of heliobiological relations, the investigations of V. B. Makeyev and V. G. Sidyakin pertaining to experimental studies and clinical observation of biological effects of magnetic fields.

In the introduction, the authors make a critical assessment of existing model conceptions of effects of space factors on the biosphere, correlation between human pathology and heliophysical factors; there is argumented validation of a new term, space ecology, in the place of the term, heliobiology, which had been proposed at one time by A. L. Chizhevskiy. Indeed, it is not only solar activity, but a number of other space factors that have an effect on living organisms. For this reason, the term proposed by the authors is appropriate, it reflects more fully the essence of space effects and should "take" in the scientific and educational literature.

Chapter 1 is a brief presentation of information about solar activity: electromagnetic and corpuscular radiation, solar activity and geophysical perturbations. The authors included a table in the summary of this chapter, which lists environmental parameters that depend on variations of solar activity and that are subsequently discussed as ecological space factors. Factors that are insignificant in the authors' opinion are omitted, such as surges of radiowaves from major sun flares, noise storms, geomagnetic field, variations in intensity of cosmic rays. We believe that these factors should not be dismissed so categorically. The methodological level of our research at the

present time is not sufficient to record the effects of these factors. We cannot rule out their role in phylogenetic development of the animal and plant kingdoms.

Chapter 2 successively discusses literature concerning the effect of ecologically relevant space factors on processes occurring in the biosphere. There is a description of the effect of solar activity on some physicochemical processes occurring in an abiotic environment. Multilevel analysis of these influences on vital activity of organisms on different levels of organization is of considerably greater theoretical and practical interest. It should be stressed that heliogeomagnetic activity is particularly relevant to a number of physiological processes: motor activity and circadian rhythms, alimentary activity, productivity and survival of animals. Established patterns are used to elaborate long-term forecasts of epizootic outbreaks of foot-and-mouth disease, tularemia, plague and others. Information about the patterns of nervous system responses to changes in the heliophysical situation, functional state of circulatory organs and the hemopoietic system as a function of changes in the geomagnetic field, effect of solar activity on dynamics of morbidity will be of special interest to clinicians.

Chapter 3 analyzes the ecological role of physical factors that depend on solar activity. The authors offer argumented validation of the complex and combined nature of effects of several variables on various processes that occur in natural ecological systems. In particular, they analyze information concerning the biological effects of atmospheric infrasound, which is one of the least studied physical factors depending on solar activity; they assess the ecological significance of increase in radon concentration in the atmosphere; they report the biological effectiveness of ultraviolet radiation in the range of 290-340 nm (B band). Analysis of existing data convince us of the appreciable ecological relevance of ultraviolet radiation, the effect of which is complex and has many steps. Finally, this chapter has information about variations that are related to solar activity in the electric field, which are of appreciable ecological significance, and about earth's electromagnetic field in the range of low and ultralow frequencies.

The logical continuation of this chapter is experimental analysis of the biological effect of weak electromagnetic fields of ultralow frequencies, which is contained in Chapter 4. The authors conducted extensive magnetobiological experiments to examine responses of the blood, cardiovascular and nervous systems. Methodologically, it is important to validate the choice of physiological criterion to describe the biological activity of a variable ultralow-frequency magnetic field. On the basis of the results of investigations, the authors concluded that high sensitivity to ultralow-frequency electromagnetic fields is a general biological feature. Not only do they analyze the obtained facts, they also try to validate the mechanism of this effect on organisms. Unfortunately, the authors did not express their critical attitude toward the numerous hypotheses concerning the primary mechanism of effect of weak electromagnetic fields, and for this reason subchapter 4.5 remained unfinished in our opinion.

Chapter 5, "Solar Activity and Biological Rhythms," was of special interest. Although the authors did not undertake a special investigation of biological

rhythms, their analysis of existing data enlarges appreciably upon our knowledge about the links between biological rhythms and solar activity (interplanetary magnetic field, electromagnetic field), as well as about synchronization of biorhythms of environmental parameters. It is regrettable that this chapter did not cover works dealing with analysis of time characteristics of biological processes authored by B. S. Alyakrinskiy, Yu. A. Romanov, G. D. Gubin and others.

The bibliography lists 539 references. The book is of interest, not only to ecologists and researchers concerned with space, but a wide range of practicing physicians, as a modern presentation of the effects of solar activity on different systems of man under normal and pathological conditions.

In conclusion, we should comment on the good quality of the printing of this book.

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BIBLIOGRAPHY OF SPACE BIOLOGY AND MEDICINE

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[Article by I. T. Akulinichev and A. A. Shipov]

[Text] The next volume of the worldwide bibliographic guide of space biology and medicine, as well as allied problems of life under extreme conditions, has been published.

This relatively young discipline, space biology and medicine, has been compiling a systematic retrospective bibliography on problems with which it is concerned from the very start of the era of manned spaceflights. The first volume of the bibliography (1961-1965) was published by "Nauka" Publishing House in 1972 [1], the second (1966-1970) in 1978 [2] and the third (1971-1975) in 1987 [3]. Bibliographies for subsequent periods will be published by the Library imeni V. I. Lenin in the form of annuals [4].

The bibliographers of the Library imeni V. I. Lenin, together with representatives of the Central Scientific Medical Library and Library of the USSR Academy of Sciences (Leningrad), under the general supervision of Ye. A. Koltun, have prepared a reference book that is quite valuable for scientific and practical work. In this edition, the guidelines for selection of works in the bibliography, their annotation and classification have been upgraded on the basis of the experienced gained by the compilers. A. A. Gyurdzhian, specialist in the field of space biology and medicine, was very helpful in compiling the bibliography; he proposed a system of classification of rubrics, offered advice and informed the compilers about the substance and details of special problems in this discipline.

The bibliography under review is a complete and fundamental edition with appropriate headings, classification and indexing of works. The bibliographic descriptions conform entirely to GOST [USSR State Standards] specifications. There are usually good translations of titles of foreign works. The guide is to be credited greatly for the fact that, in all instances where the title of a foreign work does not disclose its content, a brief annotation is furnished. The vast majority of bibliographic descriptions were prepared on the basis of reviewing original sources (de visu), and in only isolated instances were they based on abstracts. This bibliography has an author index. Unfortunately, due to its limited size, the list of serial publications and collections published in preceding volumes was omitted in the third one.

Preparation and regular publication of retrospective bibliographies are particularly necessary for rapidly developing disciplines, in particular for space biology and medicine, which is on the borderline of various biomedical, sociopsychological, engineering-technical and many other disciplines. For this reason, the existing publications dealing with relevant ranges of problems are scattered in numerous editions, which makes it difficult for specialists to gather bibliographic material.

The comprehensive heading breakdown (more than 130 rubrics), system of references and cross references permits finding readily the literature on a specific subject or works containing two or three specified concrete aspects at the same time.

It is interesting to track the dynamics of scientific problems, in which there is reflection of scientific interests in a discipline, covered in this guide. While the title of the first volume referred to only biomedical problems of spaceflights, there was reflection of sociopsychological aspects as well in the second volume, and additionally problems of exploration of regions of earth with extreme living conditions are covered in the third volume. This is indicative of the close and multifaceted interweaving of "space" and "terrestrial" science, its theory and practice, which is consistent with the current stage of accelerated social and economic development of our country and optimum use of the human factor for this purpose.

The bibliography being reviewed offers the opportunity to make a scientific analysis of publications and assess the status of different directions of our discipline, intensity of publications, basic trends in development and emerging "growth points" of interest for future planning of scientific research.

The preceding two volumes of this guide were well-rated in the periodical press. The compilers heeded many of the voiced comments and wishes. At the present time, the annuals that are being published have succeeded in shortening the gap between the year of publication of a bibliography and the last year of cited references in it.

This volume of the bibliography lists about 10,000 references published in the period of 1971-1975 (there were 4724 in the first volume and 8258 sources in the second) and, no doubt, it will be a useful reference for specialists in the most diverse fields, scientists, VUZ instructors, staffs of design offices and other scientific-practical institutions. We hope that this major and needed job of putting out bibliographies on space biology and medicine, as well as allied scientific problems, on a regular basis will continue just as successfully.

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EIGHTH ALL-UNION CONFERENCE ON SPACE BIOLOGY AND AEROSPACE MEDICINE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (manuscript received 9 Dec 86) pp 90-94

[Article by A. E. Enes and V. Yu. Kovalev]

[Text] The 8th All-Union Conference on Space Biology and Aerospace Medicine, which was organized by the USSR Academy of Sciences, jointly with the "Space Biology and Physiology" Scientific Council, Institute of Biomedical Problems of the USSR Ministry of Health and Museum of History of Cosmonautics imeni K. E. Tsiolkovskiy, convened in the Political Education Center of the CPSU Oblast Executive Committee, in Kaluga, from 25 to 27 June 1986. Prominent specialists and scientists of the Soviet Union, socialist nations, United States, France, FRG, West Berlin, Sweden and India participated in this conference.

Timely problems of interaction between living organisms and the environment--long-term accelerations, weightlessness, artificial gas atmosphere, cosmic radiation and many other extreme factors that affect man in aircraft and space missions, particularly, on orbital stations--were discussed at this conference, the slogan of which was "Contribution of space biology and aerospace medicine to Ecology."

At the plenary session, Academician O. G. GAZENKO delivered the opening remarks. He commented on the broad representation of participants at the conference, which indicates once more the importance of joining forces to solve problems of space exploration for peaceful purposes. Soviet and foreign scientists displayed much interest in the papers delivered by YE. YA. SHEPELEV, "Space, the Biosphere and Man," S. A. BUGROV, "Aviation Medicine and Safety of Pilot-Aircraft-Environment System," and A. N. VIKTOROV, "Medical Significance of Distinctions in Formation of Ecological Systems Comprising Man and Microorganisms in Habitable Environments."

There were six sections at the conference: Section No 1, "Problems of Ecology, Habitability and Hygiene"; Section No 2, "Clinicophysiological Investigations"; Section No 3, "Psychophysiological Aspects of Activity"; Section No 4, "Biology"; Section No 5, "Radiobiology"; Section No 6, "Metabolism and Its Regulation."

Soviet and foreign scientists also participated in round-table discussions. At a discussion chaired by G. M. Zarakovskiy, there was talk about problems

of technological progress and development of aerospace medicine. The discussion on the topic of "Hygienic Parameters of Habitat Environment and Man's Psychophysiological State" was chaired by E. V. Lapapyev. Current tactics and prospects for protection against space motion sickness were discussed under the chairmanship of I. B. Kozlovskaya.

At meetings of the section on "Problems of Ecology, Habitability and Hygiene," participants discussed a wide range of problems dealing with generation and maintenance of microclimate, gas atmosphere and sanitary hygienic living conditions aboard manned spacecraft, orbital stations and in model experiments (Ye. Ya. Shepelev, A. N. Viktorov, B. V. Anisimov, Yu. P. Bizin and others).

A significant number of reports dealt with the results of toxicological and microbiological tests performed aboard the Soyuz-T--Salyut-7 orbital complex and during manned spaceflights. The results of studies of biological adequacy of elements of the life-support system revealed that the generated microclimate conditions were consistent with the basic physiological requirements for vital functions. In this section, it was noted that there has still not been sufficient investigation of processes of interaction between microfactors and biological substrates on the molecular level. In discussions of the immediate tasks for space toxicology, the need for using an integral evaluation of effects of toxic agents on different systems of the body was mentioned (V. P. Savina).

Prevention of endogenous infections in crews was the topic of papers written on the basis of the results of microbiological studies (V. K. Ilyin, A. A. Lentsner, M. P. Bragina, Yu. N. Kuprin). Formation of antibiotic resistance, change in virulence of conditionally pathogenic automicroflora of man under spaceflight conditions are a threat to onset of dysbacteriosis, as well as infectious diseases in cosmonauts. Further in-depth investigation of the mechanisms of mutation and variability of human automicroflora will help expand the spectrum of drugs and optimize their action, which is aimed at maintaining ecological equilibrium between the macroorganisms and microorganism.

Maintaining immunological homeostasis during spaceflights is still an important problem. The data submitted at section meetings concerning population-related disturbances of lymphocytes with regulatory functions are a modern basis for future directions of research in the field of space immunology (I. V. Konstantinova).

Meetings of the section entitled "Clinicophysiological Investigations" dealt with current methods of expert evaluation and clinicophysiological preparation of pilots and cosmonauts, investigation of effects of spaceflight factors on different physiological systems of man, results of model experiments aimed at finding new, more effective ways and means of preventing the adverse effect on man of spaceflight factors (A. D. Yegorov, A. I. Grigoryev, U. Baldin, D. Virt, V. V. Davydov, R. M. Bayevskiy, O. G. Itsekhovskiy and others). In addition, there was discussion of problems such as medical care during spaceflights and implementation of rehabilitation measures (V. A. Bodrov, I. B. Goncharov, E. B. Petrova, B. L. Gelman and others).

Current methods of pilot and cosmonaut screening and training are based on studies of the effects on man of a set of specific factors which simulate on the ground the different factors of aircraft and space flights. The papers discussed the possibility and potential of using lower body negative pressure (LBNP), accelerations with different signs, graded physical exercise tests and rotation on a centrifuge.

At section meetings, there was extensive discussion of the results of studies pursued aboard the Salyut-7--Soyuz orbital complex, including the effects of spaceflight factors on the cardiovascular, respiratory, vestibular, skeletomuscular and other systems.

The dynamics of the tested parameters of the cardiovascular, respiratory and skeletomuscular systems of man during orbital flight, as well as at the lift-off and descent stages, were consistent with prevailing factors (A. R. Kotovskaya, F. Beysh, G. A. Fomina and others).

Many papers (in particular, at meetings of the "Clinicophysiological Investigations" section) dealt with the problem of motion sickness, its theoretical and applied aspects (S. S. Markaryan, I. B. Kozlovskaya, E. V. Lapayev, L. N. Kornilova, V. I. Kopanev and others).

Much interest was inspired by discussion of existing opinions concerning the etiology and pathogenesis of motion sickness. There was discussion of the most popular conceptions--hemodynamic and neuroreflex theories (V. I. Kopanev). The experimental data submitted in reports of Soviet and foreign scientists demonstrated the validity of discussing them. Hemodynamic changes observed in microgravity lead to change in qualitative and quantitative characteristics of afferent flow from mechanoreceptor vascular zones. In the opinion of specialists concerned with cardiovascular responses to weightlessness, this is the cause of development of specific processes of restructuring of functional systemic pattern in the function of analzyers, which is manifested by the clinical syndrome of motion sickness.

On the other hand, experimental studies of vestibular responses pursued by Soviet and American specialists confirm the conception of dominance of vestibular and visual inputs. The functional change that occurs during adaptation to weightlessness in the structure of neuronal connections of the vestibular analyzer is related to change in afferent flow from the nonacoustic part of the labyrinth, as well as visual and proprioceptive afferentation (I. B. Kozlovskaya, R. A. Solodovnikov and others).

The efficacy of steps taken to prevent motion sickness is indicative of the major contribution of extralabyrinthine, namely visceral, afferentation. In the future, investigation of mechanisms of space motion sickness will develop along the route of studying interaction between heteromodal afferent flow on different levels of the central nervous system (CNS) in order to identify preventive agents that exclude visceral symptoms.

A significant number of papers delivered in the "Clinicophysiological Investigations" and "Metabolism and Its Regulation" sections dealt with the results

of ground-based experiments simulating the effects on biological systems of weightlessness. As a model, antiorthostatic [head-down tilt] hypokinesia (HDT) of varying duration was used.

Gravity-related changes in fluid-electrolyte and mineral metabolism and their consequences are still a serious problem of space biology and medicine.

The data submitted in the papers are indicative of the systemic nature of changes that take place in bone (S. A. Bugrov, A. S. Ushakov, A. I. Grigoryev, N. P. Artamonova, L. G. Yelkina, S. M. Yerishkov and others). There was comprehensive discussion of mechanisms of impairment of processes occurring on subcellular structures of cells, metabolic disturbances, disturbances referable to enzymes of normal and neuroreflex regulation of metabolic processes.

There was extensive discussion of measures aimed at correcting fluid-electrolyte metabolism in cosmonaut crews, including those undergoing experimental testing (O. I. Orlov, V. A. Kondratyuk, I. L. Medkova, A. S. Pankova, L. V. Prilipko and others).

As shown by the results of biochemical tests on crews, the most promising direction in this area is the use of pharmacological agents that act on the membrane-molecular level in conjunction with physical exercise.

The general purpose of biomedical research conducted on the ground and in space is to provide comprehensively for active vital functions and maximum work capacity to crew members in air transport vehicles, spacecraft and orbital stations. Psychological work capacity, steps to optimize it, questions of expert evaluation and determination of the mental state of operators were discussed at meetings of the section entitled "Psychophysiological Aspects of Activity." There was comprehensive discussion of the problem of mobilizing the psychophysiological resources of the body, improving operator productivity under extreme conditions as functions of interrelated mental and physiological processes (G. M. Zarakovskiy, O. I. Zhdanov, O. P. Kozerenko, A. P. Nechayev, M. A. Novikov, A. I. Revyakin and others); psychophysiological mechanisms of active correction and formation of the operator's needs and motivations were discussed in detail: providing conditions for increased motivation with dominance of positive motivations to reach a goal, use of means of affecting the emotional area, consideration of individual personality traits, use of self-regulation and self-monitoring methods.

Evaluation of the mental status of operators, which is made at all stages of pilot and cosmonaut work, is still a pressing problem. Use of conventional and modern methods permits a comprehensive evaluation of the operator's mental state, on the basis of individual psychophysiological distinctions, as well as prediction of the nature of an operator's behavior under extreme conditions.

Computerization of research, development of biomedical cybernetic complexes, constitutes a promising potential, which affects literally all directions of aerospace biology and medicine (R. M. Bayevskiy, A. A. Glushko). It was noted at the meetings that further development of computerization and use of cybernetics in biomedical research is related to improvement of software, a search for new physicotechnical effects, optimization of methods and standardization

of measuring equipment. Development of a measurement-information system coordinated with an automated bank of data pertaining to physical environmental factors, biophysical effects, physiological characteristics of the body and other active data filies is a promising direction.

Many of the papers delivered in the "Biology" section dealt with biological systems of living organisms under spaceflight condtiions and in model experiments.

It is obvious from the reports submitted in this section that all of the changes in the animal circulatory system caused by spaceflight factors can be viewed as a compensatory response called upon to provide for rapid hemodynamic adaptation (V. P. Krotov et al., A. M. Badakva et al.).

A decline of strength characteristics of bone in the animal skeletomuscular system was demonstrated, which is attributable to decrease in amount of crystalline hydroxyapatite and accumulation of amorphous calcium phosphates (A. V. Bakulin et al.). The changes in skeletal muscles under the effect of microgravity, which are both systemic and differentiated in nature, are due to the following causes: involvement of an additional number of motor units to perform the same task because of diminished force of contraction of individual fibers; change in central mechanisms of control of movement and sequence of activation of motor units; worsening of circulation (V. S. Oganov et al., S. A. Skuratov et al.).

During a spaceflight, the central nervous system of living organisms is constantly exposed to psychogenic stimuli, which lead to change in dynamics of secretion of biogenic amines, glucocorticoids and androgens in monkeys and specific substrates of the rat brain (V. I. Drobyshev, T. G. Stepanov, V. Yu. Kovalev, A. E. Enes), which may be associated with functional changes in the CNS. For this reason, the problem of enhancing resistance of this biological system to emotional stress. It is being solved with the use of various psychotropic agents, among which pyrroxan has the maximum protective effect; its administration prevents development of emotional stress, as well as concomitant behavioral, visceral and neuroendocrine changes (A. M. Chirkov and others). Phenolin and piperidine ethylselenophene enhance significantly rat resistance to audiogenic seizures (L. L. Stazhadze and others).

High stability is inherent in some of the biological systems of animals and man. Spaceflight factors had no effect on fluid-electrolyte homeostasis of developing rat fetuses or on radiation mutagenesis in female Drosophila (Ye. A. Lavrova et al., A. V. Smirnova).

Investigation of changes in biological systems of plants under spaceflight conditions is of great practical importance to future exploration of space. Thus, temperature changes could have an appreciable effect on physiological and genetic parameters (V. P. Zhalikovskaya). The heavy component of cosmic radiation elicits decrease in capacity for cell repair (L. N. Kostina et al.). All of the changes have species-specificity (Z. K. Abilov et al.).

The immediate plans of space biology are to pursue deeper investigation of the effects of spaceflight factors on living organisms as a whole and on their different systems, as well as development of closed ecological systems.

At meetings in the "Radiobiology" section, there was extensive discussion of the conception of risk in setting standards for radiation safety of spaceflights (Ye. Ye. Kovalev, V. A. Sakovich). In this regard, the paramount role of the set of "Safety, Radiation, for spacecraft Crews During Spaceflights" GOST's, which was elaborated by Soviet scientists (V. A. Sakovich et al.) was noted.

A significant number of papers dealt with investigation of the effects on biological systems of radioactive radiation. Until recently, it had not been determined whether increase in intensity of ultraviolet fluorescence of leukocytes of blood and bone marrow occurs in man. The studies of A. S. Yagunov warrant the belief that the increase in intensity of ultraviolet fluorescence of leukocytes is a general response inherent in all mammals.

A number of papers was concerned with investigation of the effects of radiation on biological systems. According to the papers of A. Bayrokov et al. and I. N. Ryzhov et al., cytogenetic changes in mouser reproductive cells and physical work capacity of rats were a distinct function of radiation dosage at all postexposure terms. There was a decline in rate of recovery of spermatogenesis parameters with increase in dosage. Repeated exposure to neutrons had an aggravating effect on production of mouse spermatogenic epithelium (N. L. Fedorov, A. V. Shafirkin).

It is of great interest to study the effect of the adaptation process on resistance to extreme factors, in particular, ionizing radiation. In this respect, the report of Yu. V. Farber merits attention; it indicates that adaptive responses that occur with change in ambient conditions are reflected in resistance to extreme factors. With increase in adaptation time, sensitivity to stressors diminishes. In the opinion of I. A. Aleshin, diminished expression of a radiation effect can be obtained by breathing air with low partial oxygen pressure, which can be viewed as an individual means of protection against radiation under appropriate economic conditions and in extreme situations.

A number of papers was concerned with the study of the effects of radiation on plants. The reserach results submitted indicate that the disturbances noted in plant cell structures are linear, and they are related to absorbed dose (Yu. A. Akatov et al.). In addition, secondary proton radiation plays a substantial role in formation of the observed radiation effects (L. N. Kostina), while the anomalous phenomena that occur persist in the next generation (V. M. Abramov, A. M. Marennyy).

At the meeting of the "Radiobiology" section, in addition to discussion of the experimental findings, questions were raised pertaining to future research. Experimental investigation of the effects of impact waves on biological systems merits attention, with respect to evaluation of the radiation hazard of heavy charged particles. Preliminary experiments with simulation of the impact wave from a track and its effect on biochemical systems confirmed the need for further investigation of this effect, in order to explain the observed effects of the heavy component of galactic cosmic rays on biological systems (Ye. Ye. Kovalev, O. D. Bril, Ye. Ye. Kovalev et al.).

The material presented at the 8th All-Union Conference on Space Biology and Aerospace Medicine constitutes, in essence, the results of 4 years of work done by scientists and specialists of different countries.

The results of research in aerospace physiology and medicine have made it possible to elucidate the substance and mechanisms of functional and structural changes that occur during spaceflights, as well as to undertake development of more effective preventive and therapeutic methods. The general conclusion for this direction of research is that there is reversibility of functional changes that take place under the effect of spaceflight factors. Not only the possibility of long-term stays in space, but efficient performance of cosmonauts in space, are a corollary and confirmation of this statement.

Acceleration of scientific and technological progress, the more complex control systems of modern aircraft and space equipment put tasks to psychology that require immediate resolution. The methods discussed at this conference for improving psychophysical screening of flight personnel as candidates for cosmonauts, operator training for working under extreme conditions, as well as the new ergonomic requirements of the man-machine system, will no doubt find application in the practice of aviation and space medicine.

Problems of habitability and radiation protection, which were discussed at the conference, are based on fundamental research in space biology. Soviet and foreign scientists summed up the results of scientific research, discussed the means of solving new problems in the area of radiobiology and habitability at section meetings.

The conference participants visited the K. E. Tsiolkovskiy Museum and Museum of History of Cosmonautics imeni K. E. Tsiolkovskiy.

During this conference, there was a concurrent reader conference of the journal, KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA. In a meeting of the editorial board of this journal with readers, N. N. Gurovskiy, deputy editor in chief, acquainted the participants of the readership conference with the tasks put to the journal. Readers were handed out a questionnaire in order to further improve the performance of the journal.

On the whole, the conference was on a high scientific and methodological level. The systems analysis approach, cintegral method of problem solving on the boundary between different scientific disciplines, profound basic work on pressing problems, real benefit to practical health care--all this characterizes the present contribution of space biology and aerospace medicine to the teaching on ecology, and this was vividly reflected in the work of the conference.

ANNIVERSARIES

UDC: 613.693:92 Gurovskiy

NIKOLAY NIKOLAYEVICH GUROVSKIY CELEBRATES HIS SEVENTIETH BIRTHDAY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (signed to press 23 Jun 87) pp 94-95

[Text] Nikolay Nikolayevich Gurovskiy, doctor of medical sciences, recipient of the USSR State Prize, participant in the Great Patriotic War, retired colonel in the medical service, veteran of aviation medicine and one of the founders of space medicine in the USSR, celebrated his 70th birthday on 2 May 1987.

N. N. Gurovskiy has traveled a glorious road as citizen and communist, physician and warrior, scientist and science organizer.

Upon graduating in 1940 from the Military Faculty of the Second Moscow Medical Institute, he served as a physician for many years in several aviation medical units (chasti and soyedineniya). While on duty at the Airforce Engineering Academy imeni N. Ye. Zhukovskiy, N. N. Gurovskiy worked on upgrading functional diagnostics and evaluation of human health, along with studying medical support of Academy personnel.

In 1951, N. N. Gurovskiy enrolled for graduate studies in the department of aviation medicine of the Central Institute for Advanced Training of Physicians, where he conducted a rather interesting investigation of the effect of vibration of the MI-4 helicopter on pilots, under the guidance of A. P. Popov, F. G. Krotkov and D. Ye. Rozenblyum. After defending his dissertation, he remained in this department to continue with his research.

In 1959, N. N. Gurovskiy head work, initiated in the Soviet Union for the first time, on screening and training cosmonauts for future missions. The bases and guidelines of this work, which were advanced by N. N. Gurovskiy and his associates, have retained their relevance to this day. In 1970, he successfully defended his doctoral dissertation.

In 1964, N. N. Gurovskiy was appointed chief of the Administration for Space Biology and Medicine of the USSR Ministry of Health. In this period, USSR space medicine achieved major successes.

N. N. Gurovskiy has been working since 1981 first as deputy and then as assistant director for scientific organization work at the Institute of

Biomedical Problems of the USSR Ministry of Health. He does much work in the area of dissemination, editing and publication of the principal results of biomedical investigations of space. As deputy editor in chief of KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA, he is making an inestimable contribution to implementation of ongoing work and refinement of this journal.

N. N. Gurovskiy has othered more than 150 original research and theoretical works. The Party, government and Federation of Cosmonautics have rated highly his noble work, having bestowed many orders and medals upon him.

The friends, coworkers and disciples of N. N. Gurovskiy appreciate highly and love Nikolay Nikolayevich for such exceptional personality traits as kindness, responsiveness, wisdom, principle-mindedness, and wish him many more years of happy live and fruitful scientific, scientific-organizational and public endeavors.

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VASILIY ILYICH KOPANEV (SIXTIETH BIRTHDAY)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 21, No 4, Jul-Aug 87 (signed to press 23 Jun 87) pp 95-96

[Text] The 5th of June, 1987 marked the 60th birthday and 38th year of medical, scientific and public service for Professor Vasiliy Ilyich Kopanev, doctor of medical sciences, member of the editorial board of the journal, KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA.

V. I. Kopanev was born in 1927 in Kirov Oblast. He graduated in 1949 from the Naval Medical Academy and in 1954, from the Soil Biology Faculty of Leningrad University imeni A. A. Zhdanov, thus having gained the qualifications of physician and physiologist.

Having attended a course for advanced training with Prof M. P. Brestkin, he began in 1954 his scientific endeavors with enthusiasm; they pertaining to first aviation and then space medicine. His first scientific publication was the article, "Gastric Secretory Function in the Presence of Motion Sickness."

In 1961, V. I. Kopanev defended his candidatorial dissertation on the topic of "Functional State of the Visual Analyzer in the Presence of Motion Sickness," and in 1970, his doctoral dissertation on the topic of "Problem of Statokinetic Stability of Man in Aviation and Space Medicine," in both of which he summarized data on the problem of motion sickness.

He is to be credited with the first description of a latent form of motion sickness, expanded interpretation of the problem of statokinetic stability of man from the standpoint of functional systemic nature of central nervous system function.

His good theoretical training, comprehension of distinctions of spaceflights, great experience in conducting scientific research and ability to define the main directions enabled V. I. Kopanev to complete several studies on the problem of weightlessness, which are important to space medicine.

The results of this research were published by him, together with a team of authors, in several collective monographs: "First Manned Spaceflights" (1962), "First Spaceflight by a Team" (1964), "Second Spaceflight by a Team" (1965), "Space Biology and Medicine" (1966), "Weightlessness" (1974) and "Bases of Space Biology and Medicine" (1975).

V. I. Kopanev has authored more than 200 scientific works, including monographs, textbooks and methodological guides for aviation physicians.

He devotes much attention to training and education of scientists. A total of 18 candidatorial dissertations were prepared and successfully defended under his guidance. His disciples are working at various scientific research and educational institutions, heading laboratories, departments and special courses (V. Ya. Lopukhin, I. K. Tarasov, I. A. Kolosov, D. T. Lukashchuk and others).

In recent years, V. I. Kopanev has devoted much attention to training aviation physicians, heading a department at the Military Medical Academy imeni S. M. Kirov.

V. S. Kopanev is very involved in public service, being a member of the editorial board of our journal, member of the editorial board of the Great Medical Encyclopedia, chairman of the Leningrad Section of Aviation and Space Medicine of the All-Union Physiological Society imeni I. M. Sechenov.

The performance of V. I. Kopanev has been rewarded with state awards.

On the day of his 60th birthday, the editorial board of this journal offers its sincere congratulations and wishes him further creative achievements.

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